Vol. 9 JUNE, 1934 No. 5

Hospital Library

THE AMERICAN HEART JOURNAL

© Am. Ht. Assn.

ADVISORY EDITORIAL BOARD

E. P. CARTER
HENRY A CHRISTIAN
ELLIOTT C. CUTLER
WALTER W. HAMBURGER
JAMES B. HERRICK
WILLIAM J. KERR
SIR THOMAS LEWIS
E. LIBMAN
H. M. MARVIN
JONATHAN MEAKINS
JOHN H. MUSSER
JOHN ALLEN OILLE
STEWART R. ROBERTS
G. CANBY ROBINSON
FRED M. SMITH
PAUL D. WHITE
CARL J. WIGGERS
FRANK N. WILSON
CHARLES C. WOLFERTH

PUBLISHED BI-MONTHLY
UNDER THE EDITORIAL DIRECTION OF
THE AMERICAN HEART ASSOCIATION

LEWIS A. CONNER - - - - - Editor
Associate Editors
HUGH McCULLOCH
EVELYN HOLT

PUBLISHED BY THE C. V. MOSBY COMPANY, 3523-25 PINE BLVD., ST. LOUIS, U. S. A.
Entered at the Post Office at St. Louis, Mo., as Second Class Matter.

The American Heart Journal

CONTENTS FOR JUNE, 1934

Original Communications

Coronary Arteries in Rheumatic Fever. Howard T. Karsner, M.D., and Francis Bayless, M.D., Cleveland, Ohio 557

Incidence and Significance of Active Infection in Cases of Rheumatic Cardiovalvular Disease During the Various Age Periods. M. A. Rothschild, M.D., M. A. Kugel, M.D., and Louis Gross, M.D., New York, N. Y. 584

The Form of the Electrocardiogram in Experimental Myocardial Infarction. I. Septal Infarcts and the Origin of the Preliminary Deflections of the Canine Levocardiogram. Frank N. Wilson, M.D., Ian G. W. Hill, M.B., and Franklin D. Johnston, M.D., Ann Arbor, Mich. 596

The Initial Complex of the Electrocardiogram After Infarction of the Human Heart. Max Winternitz, M.D., Prague, Czechoslovakia 616

The Duration of the QRS Complex in the Normal and in the Abnormal Electrocardiogram. Sylvester McGinn, M.D., and Paul D. White, M.D., Boston, Mass. 642

Dynamic Dilatation of the Thoracic Aorta. W. K. Purks, M.D., Boston, Mass. 655

An Electrocardiographic Study of Viscerocardiac Reflexes During Major Operations. C. C. Maher, M.D., P. J. Crittenden, Ph.D., and P. F. Shapiro, M.D., Chicago, Ill. 664

Department of Clinical Reports

Observed Onset of Bundle-Branch Block With Coronary Thrombosis 45 Hours Later. C. Bruce Perry, M.D., Bristol, England 677

Hemopericardium. Bernard I. Comroe, M.D., Philadelphia, Pa. 680

Syphilitic Aortitis With Aneurysm of the Innominate Artery and Occlusion of the Left Common Carotid Artery. Laurence E. Cooley, M.D., and Frank P. McNamara, M.D., Dubuque, Iowa 686

Department of Reviews and Abstracts

Selected Abstracts 690

Book Review 696

The American Heart Journal

VOL. 9 JUNE, 1934 NO. 5

Original Communications

CORONARY ARTERIES IN RHEUMATIC FEVER*†‡

HOWARD T. KARSNER, M.D., AND FRANCIS BAYLESS, M.D.
CLEVELAND, OHIO

INTRODUCTION

THE fact that in the course of infectious diseases lesions of the blood vessels may occur has long been known. Suppurative inflammations may originate in any coat of an artery, due to blood dissemination of bacteria or as the result of direct extension of an inflammation. Less familiar are changes whose origin is uncertain and whose nature is disputed. It is probable that poisonous products of bacteria may produce vascular degeneration. In the case of those diseases now believed to be of allergic nature similar degenerations occur. In the allergic conditions Roessle (1933) has offered the assumption that the vascular lesions are part of a general mesenchymal reaction. There is, however, the possibility that since allergic processes represent antigen-antibody reactions, the meeting of these bodies may occur especially at the junction of blood and tissues in the vessels. This is suggested by the experiments of Apitz (1933) who found that when hemorrhage follows the application of crotalus venom it is due to the meeting at the capillary walls of the venom and the activating substances contained in the circulating blood. The fact that the supposed allergic inflammatory reaction in small arteries occurs especially in media and adventitia is probably explained by the experiments of Ramsey and Alpert (1933) who found that injury of the intima by turpentine or croton oil produces reaction only in the outer media and in the adventitia.

The nature of the process may be clearly degenerative or clearly exudative. In connection with the former, proliferation, especially of con-

*From the Institute of Pathology, Western Reserve University and University Hospitals, Cleveland.

†Aided by a grant from the Josiah Macy, Jr., Foundation.

‡Presented in abstract before the Association of American Physicians, Washington, D. C., May 9, 1933.

nective tissue, occurs; and there is an academic question as to whether this is a substitution process, merely reparative, or a progressive fibrosis of inflammatory nature. It is our view that the proliferation is progressive. Thus the degeneration and proliferation would constitute an alterative type of inflammation.

VASCULAR DISEASE IN GENERAL INFECTIONS

The earlier studies of Hayem (1869, 1870), of Martin (1881, 1883), Huguenin (1883), Landouzy and Siredey (1885, 1887), Therese (1893), Hanot (1894) and others drew attention to acute vascular degeneration, sometimes with endarterial proliferation, in general infectious diseases. The detailed study of the microscopic anatomy was made by Cowan (1904), who described intimal proliferation, round cell infiltration of the media and adventitial fibrosis of coronary arteries in many general infections. Wiesel (1906) laid more emphasis on degenerative changes especially in the media of the coronaries, with serous infiltration and necrosis. He described swelling and rupture of the elastica interna, intimal proliferation, and fibrosis, which he interpreted as scarring. He found that typhoid fever, diphtheria and influenza injured the elastica more severely than did scarlatina and septicopyemic diseases. Wiesner (1906) confirmed these observations and extended them to include eclampsia, endocarditis and congenital syphilis. Frothingham (1911) reported intimal thickening and fat droplets in intima and media in various arteries in general infections.

Wiesel and Loewy (1919) in a study of peripheral arteries in acute and chronic circulatory insufficiency, found coronary lesions only when other peripheral arteries were affected. They attributed the vascular lesions to earlier infectious diseases and were definitely of the opinion that the fibrosis is not inflammatory but reparative and may be accompanied by muscle regeneration. Nevertheless they suggested that the acute arterial disease may be the precursor of arteriosclerosis. Stoerk and Epstein (1920), in their study of the arteries in grip, reported medial changes like those described by Wiesel and Loewy, fatty degeneration of the intima, and sometimes a calcification of fragmented elastica. They emphasized muscle regeneration and considered the fibrosis to be compensatory to weakening of the wall, according to the old Thoma theory. MacLean (1929) and Klotz and Lloyd (1930) have given clear evidence of the influence of infectious disease in the production of degeneration, inflammation and fibrosis of the coronary arteries. It has been suggested that the medial disease may lead to aneurysm formation or rupture, and Gastewa (1933) has reported a case of cerebral hemorrhage believed to be due to the vascular lesion of typhoid fever.

It may be said that general infectious diseases are capable of producing degenerative, exudative and proliferative lesions of the arterial system.

The reports of Mandelstamm (1932) and Gouley, Bellet and McMillan (1933) on tuberculous arteritis, Seifried and Cain (1932) on arterial lesions of hog cholera, Hansmann and Schenken (1932) on melitensis meningo-encephalitis, Schenken and Hansmann (1932) on intestinal arteries in mercuric chloride poisoning, of Lillie (1932) on Rocky Mountain spotted fever, and Gerstel (1933) on pneumonoconiosis, indicate that no sharp line can be drawn between degenerative and inflammatory lesions. This is emphasized in the study of polyarteritis nodosa by Klinger (1931), who in an examination of 2 cases found in one pronounced exudation and in the other degeneration and fibrosis, but with an overlapping of the different types of lesion in both cases.

One feature of the degeneration, namely, edema of the media with separation of muscle cells and granular precipitate, has been questioned. Scharpf (1909) thought it to be not pathological. Segre and Kellner (1921-22) found it to be common in various types of disease and demonstrated that it is not postmortem artefact. They hypothecated that agonal contraction of the artery presses plasma into the walls, but they do not defend the mechanical objections nor explain why the supposed plasma is usually basophilic. Schultz (1927), however, accepted their view. Our studies usually indicate that edema is related to, or identical with, the chromotropic substance of arteriosclerosis and of idiopathic medial necrosis (Moritz, 1933).

The intimal thickening is usually cellular but may be acellular, and its nature as it affects the smaller arteries is difficult to determine. In spite of reports that it is fatty, technical limitations render this difficult to determine. It is only in extremely small part chromotropic. Krompecher (1930) believed it to be an elastica "hypertrophy," but it does not regularly stain specifically. Whether the cells which participate in the thickening are endothelial, subendothelial fibroblasts, medial fibroblasts growing through ruptured elastica, or are the hypothetical elastoblasts of Krompecher has not been determined. That the presence of elastoblasts must be assumed to explain apparent hyperplasia of elastica is not borne out by the studies of Bloom (1929), who found elastica proliferation in tissue culture without cell participation. This would indicate that at least some of the fraying of elastica is proliferative. The studies of McMeans (1915) show that fraying can be degenerative, resulting from solution of the outer sheath of the fibers. As contrasted with fraying, swelling and fragmentation must certainly be degenerative. Provided the possibility be kept in mind, we disagree with Stoerk and Epstein (1920) that fragmentation is difficult to distinguish from normal fenestration.

VASCULAR LESIONS IN RHEUMATIC FEVER

That rheumatic fever may produce arterial lesions like those of other infectious disease is well known. De Mussy (1872) and Martin (1883)

made this suggestion, as did Legroux (1884), Hannot (1894) and Astier (1897).

Rabé (1902) described a proliferative endarteritis in association with medial edema. Takayasu (1909) interpreted this endarteritis hyperplastica as the result of organization and canalization of emboli, but Geipel (1909) regarded it as an irritative intimal proliferation in response to emboli. In our opinion, neither of these explanations is satisfactory because the evidence is plainly against its origin from either thrombosis or embolism. Gräff (1929) explained the fibrosis as being due to proliferative thickening of pre-existent capillaries, but this cannot well be harmonized with the mature development of arterial structure actually observed. Geipel (1909) described endothelial and collagenous hyperplasia in the intima, fibrin deposit in the subintimal connective tissue, marked narrowing of the lumen, and destruction of elastica interna. Intimal fibrosis was also noted by Klotz (1912), Coombs (1924), Sacks (1925-26) and others. Subsequent to their reports on aortic lesions (1923-24) Pappenheimer and Von Glahn (1927) described lesions in aortic vasa vasorum like those described in peripheral arteries by Von Glahn and Pappenheimer (1926). These findings were much like those of Geipel, but with some differences and given in greater detail. The intimal lesions observed were swelling and basophilia of the endothelium, the endothelial layer often elevated by coagulated exudate between it and the elastica. They described swelling, beading, and destruction of elastica interna. In addition they noted infiltration of a few wandering cells and polymorphonuclears into a loose intimal tissue in a coronary artery. Kugel and Epstein (1928) described intimal proliferation and increased lamellation of elastica in the vasa vasorum of the pulmonary artery, not considered to be specifically rheumatic and perhaps common to infectious diseases. Similar lesions have been described in the small divisions of the pulmonary artery by Paul (1928), Eiman and Gouley (1928), and McClenahan and Paul (1929). Gray and Aitken (1929) found widespread thickening of small arteries, principally by intimal fibrosis, sometimes eccentric and usually hyalinized.

MacCallum (1925) described multiple thrombosis which he attributed to primary vascular disease, a view evidently shared by Sacks (1925-26), v. Santha (1932) and others, including ourselves. The supposition of Takayasu (1909) and Geipel (1909) that emboli are sufficiently frequent to cause the widespread intimal lesions observed is not consistent with the actual occurrence of embolism in rheumatic fever.

Medial lesions vary from edema to necrosis and ultimately fibrosis. Rabé (1902) described a vacuolated state of the media, an "état reticulaire," which he attributed to degeneration and liquefaction. This occurs in numerous other conditions, as was recognized by Rabé, and is probably edema rather than liquefaction. Actual necrosis has been ob-

served and was described by Sacks (1925-26) in renal arteries. Von Glahn and Pappenheimer (1926) described extravasation of blood, which they attributed to the vascular necrosis. Edema and chromotropic change and fibrosis have been discussed above as related to infectious disease in general, and there is no reason for assuming that they operate differently in rheumatic fever. The special relation of fibrinoid degeneration to rheumatic fever has been emphasized by Klinge (1930, 1931) but, as indicated in the discussion of hyperergy below, this may occur in other conditions. He found that it originated in the intima and extended into the media, but in our experience it is far more common in media than in intima. Infiltration of lymphocytes and large mononuclears and sometimes polymorphonuclears has been described by many writers, but is generally regarded as an extension from similar infiltrations in the adventitia.

Cell infiltration in the adventitia was well described by Von Glahn and Pappenheimer (1926), who found that an infiltration of irregularly shaped mononuclear and polymorphonuclear cells may be followed by infiltration of lymphocytes and plasma cells. Klotz (1912) assumed that the cells originally in the adventitia infiltrate into the media by way of lymphocytes. This seems to be especially true in large arteries with vasa vasorum, which in the media may be encircled by the infiltrate. MacCallum (1925) found large cells in the adventitia, but appears to have associated these with intravascular thrombi. Aschoff (1906) noted the extension of submiliary nodules into the coronaries, a feature further described by Coombs (1907, 1908-09, 1911). Generally this involvement is confined to the adventitia, but it may extend into the media. Wätjen (1921) has described actual destruction of elastica in the course of this penetration. Swift (1924), MacCallum (1925), and others have referred to compression of coronaries by the submiliary nodules, a matter discussed subsequently in this paper. Many observers have reported on fibrosis in the adventitia.

Of the larger vessels, the pulmonary artery has been studied by Paul (1928), Eiman and Gouley (1928), Kugel and Epstein (1928), McClenahan and Paul (1929), Chiari (1930, 1931), and others. The lesions in the vasa vasorum are like those of other small arteries in rheumatic fever. There is perivascular infiltration of large mononuclears, often irregular in outline, and a relatively smaller number of lymphocytes. This sleeve of cells accompanies some of the vasa into the media, where it is accompanied by destruction of elastica and muscle. Splaying and fragmentation of the elastica interna are accompanied by variable degrees of intimal fibrosis.

Klotz (1912) described the aortic lesions of rheumatic fever as penetration into the media of vasa vasorum, edema, interruption of medial elastica and muscle, perivascular infiltration of plasma cells and lympho-

cytes, together with diffuse and perivascular infiltration of plasma cells and lymphocytes into the adventitia. Pappenheimer and Von Glahn (1923-24, 1926) believed that they could identify cells in adventitia and also in media as typical Aschoff cells and described Aschoff nodules in the adventitia. They were of the opinion that the aorta may be affected primarily by way of the intima as well as through the vasa vasorum. Giraldi (1929) confirmed Klotz' observations and noted intimal proliferation in the vasa vasorum. Chiari (1928), Laubry and associates (1930) and others have reported similar findings. Barnard (1929) described ringlike fibrosis of the aortic adventitia, but did not establish his case as definitely rheumatic. Schulz and Klinge (1933) have set up criteria for the diagnosis of chronic aortitis of rheumatic origin.

That medial destruction may be of especial import is indicated in the report by Gray and Aitken (1929) of a dissecting aneurysm of the aorta, presumably of rheumatic origin. Lisi's (1930) hepatic artery aneurysm was probably mycotic rather than the result of rheumatic arterial disease. Dawson (1933) found definite vascular lesions in the subcutaneous nodules of both rheumatic fever and rheumatoid arthritis. Coburn (1933) attributed multiple small hemorrhages to rheumatic vascular disease. Craeuin and associates (1933) in their review accept the existence of rheumatic disease of smaller arteries and coronaries.

Relation to Hyperergy.—The general character of rheumatic fever as a hyperergic reaction has been considered by Swift, Derick and Hitchcock (1928). The extensive studies of Klinge have supported this hypothesis. The pathogenesis of the lesion in vessel walls, as in other structures, was summarized by Klinge and Vaubel (1931) as (1) swelling of the connective tissue ground substance with variable degrees of fibrinoid change, (2) growth or hyperplasia of the connective tissue cells with or without basophilia of the cytoplasm, accompanied by variable degrees of lymphocyte leucocyte inflammation, (3) hyaline scar formation with or without elastica destruction. The connective tissue injury was not thought to be absolutely specific for rheumatic fever. They pointed out, however, that the fibrinoid change is found otherwise only in periarteritis nodosa, malignant sclerosis, certain forms of cardiovascular sepsis, Buerger's disease and focal glomerulonephritis. These may all be hyperergic manifestations. Although they claimed that experimentally multiple injections of streptococci are required for the production of fibrinoid, Apitz (1933) found it following repeated injections of serum; Henschen (1927) described it in areas of prolonged passive hyperemia; and Therese (1893) is quoted as having produced it by single injections of bacteria.

Fahr (1930) expressed the view that Klinge had not sufficiently demonstrated the similarity of experimental hyperergy and rheumatic fever,

but Metz (1931) was in complete agreement with Klinge as was Apitz (1933) and in essence also Klotz and Lloyd (1930), and Semsroth and Koch (1930).

CORONARY ARTERIES IN RHEUMATIC FEVER

The fact that coronary arteries are involved is indicated by studies quoted above. The frequency of the coronary lesions has been the subject of differences of opinion. Klotz (1912) stated that the finer ramifications of the coronaries are invariably affected, a view shared by Coombs (1924), but MacCallum (1925) regarded coronary disease as uncommon save in severe cases. Only a few studies have been directed to this phase of the problem.

Perry (1929-30) examined in detail the large coronaries of nine patients, from five to nineteen years of age, one of whom had had angina. Involvement was noted in all. The intima showed patchy or diffuse thickening by a loose tissue, which often was acellular or showed lymphocyte infiltration near the media. The elastica interna varied greatly—from practically normal to marked splaying sometimes so bulky as to suggest proliferation. Intimal fibrosis was variable. In the media he observed loss of nuclei, the "état reticulaire" of Rabé, infiltration of lymphocytes often in a hyaline matrix. Fibrosis occurred principally in the inner half of the media in communication with intimal fibrosis. The adventitia showed fibrosis and lymphocyte infiltration of variable intensity. Fatty change was not present.

Klinge (1930) in describing the early collagenous swelling of the connective tissues in rheumatic fever referred to the same change in coronary arteries, together with the production of fibrinoid in the intima with extension into the media, sometimes accompanied by a leucocyte lymphocyte reaction, and with narrowing of the lumen. Those changes led to dissociation of the fibrous and muscle cells. He later (1931) described the subsequent states of infiltration of cells like those of the submiliary nodule, most often in the adventitia but involving in some instances the other coats. He suggested that some of the intima lesions might represent organization of thrombi. The whole process led to fibrosis. He found elastica changes in those instances of granuloma formation within the arterial wall.

Relation to Other Similar Vascular Diseases.—It is difficult to orient the vascular lesions of rheumatic fever in the whole group of arterial diseases. Aschoff (1906), Ophüls (1923), and others have suggested a relation between the lesions of rheumatic fever and polyarteritis nodosa. Fahr (1920) suggested that rheumatic arterial disease may play a part in the etiology of malignant sclerosis and (1921) drew attention to the resemblance between the arterial lesions of rheumatic fever, polyarteritis nodosa and dermatomyositis (polymyositis). Gruber (1923, 1925) be-

lieved polyarteritis nodosa to be a manifestation of hyperergic reaction. Klinge and Vaubel (1931) appear to have considered that periarteritis nodosa, malignant sclerosis, certain forms of cardiovascular sepsis, thromboangiitis obliterans, focal glomerulonephritis and rheumatic fever are grouped together on the basis of hyperergic etiology. Semsroth and Koch (1930) as well as Metz (1931) expressed the view that the arterial lesions of acute infectious diseases, rheumatic fever, and polyarteritis nodosa are manifestations of the allergic state which differ only in degree of involvement. Klinger (1931), an adherent of the Ricker school, did not share in this assumption. Jäger (1932) placed the juvenile form of thromboangiitis obliterans in this general category.

v. Santha (1932) and others considered the vascular lesions of chorea as identical with those of rheumatic fever, which is true of our experience. We agree with his view that thrombi are secondary to lesions of the vessels rather than that they are emboli from heart valves.

Relation to Arteriosclerosis.—The significance of infectious disease in the origin of arteriosclerosis is debatable, and MacCallum (1933) believed that there is insufficient evidence for such an assumption. Klotz (1914-15, 1915) adhered to the inflammatory origin of arteriosclerosis and with Lloyd (1930) expressed the view that infectious diseases including rheumatic fever are of importance for the inception of coronary sclerosis, a view shared by MacLean (1929), Siegmund (1929), Giraldi (1929) and Laubry (1930). Wiesel (1923) specifically attributed juvenile sclerosis to rheumatic lesions of the media, but this view is not accepted by Zeek (1932), who, however, found that rheumatic heart disease predisposes to early development of atheromatous lesions of the coronary arteries. Schulz and Klinge (1933) have described a chronic fibrous rheumatic aortitis, which is in reality a form of arteriosclerosis.

Relation to Myocardial Disease.—The question as to whether or not the coronary arterial lesions are the cause of myocardial damage of rheumatic fever has been discussed extensively. Hayem (1869, 1870) suggested it, and Krehl (1890) and Romberg (1894) considered it to be of great importance. This was combated by Aschoff (1904) and Aschoff and Tawara (1906), who also doubted the relation of the myocarditis to cardiac weakness. Fahr (1921) and Swift (1924) were definitely of the opinion that interference with myocardial nutrition from rheumatic disease of the smaller coronaries can cause myocardial insufficiency, and Klotz (1926) was equally certain that the myocardial scars are largely the result of the vascular disease. Slater (1930) attributed the scars to both arterial disease and direct inflammatory destruction of muscle. Brown (1932) found little evidence to support the view that the scarring results from inflammatory destruction and concluded that coronary disease is the most important etiological factor. Of her 115 cases, 15 were associated with rheumatic fever.

Disturbance of Cardiac Rhythm, and Pain.—Although case reports had previously appeared, the paper by Parkinson, Gosse and Gunson (1919-20) directed attention to the fact that irregularity of the heart action is common in rheumatic fever, and they attributed delayed conduction to myocardial inflammation. Cohn and Swift (1924) confirmed and amplified this report. Swift (1924) stated that interference with the circulation must lead immediately to disturbed nutrition of the muscle tissue and of the impulse-conducting fibers supplied by the involved blood vessels. Besançon and Weil (1926) described in detail auriculoventricular dissociation. Swift (1928) noted that arrhythmias are found in various types of infectious disease but are especially common in rheumatic fever, a view evidently shared by Lukomski (1932, 1933) and others. Slater's case is probably one of extensive infarction. Levy and Turner's (1929) report is representative of the modern view of the subject. They noted the frequency of disturbances of auriculoventricular conduction in rheumatic hearts and found that delay is more common than complete block. Although usually temporary, the disturbances may persist for a long time after subsidence of the acute rheumatic cycle. They expressed the view that in the absence of syphilis or of digitalis administration, the occurrence of prolonged P-R interval or of block in patients less than thirty-five years of age is presumptive evidence of rheumatic heart disease. They suggested that the occurrence of leucocytosis in the active stages indicates that the functional disorder may be attributed to myocardial damage, the result of occlusion of arterial twigs. Oettinger and Neslin (1932) found 14 cases of A-V dissociation in 200 cases of rheumatic carditis. This lasted usually only a few days. Their explanation was a hypothetical irritation of Tawara's node or of the automatic function of the sinus node.

Coronary occlusion is not a frequent complication of rheumatic fever. Wearn (1923) found a positive history in only one of his 19 cases, Levine and Brown (1929) in only three of 145 cases. Conner and Holt (1930) did not mention it in their large series. White and Jones (1928) mentioned it in one of 71 cases. Kerr, Larkey, and Larsen (1924) recorded definite rheumatic involvement in their four cases. Breitnecker (1931) has described a fatal case of thrombosis in the rheumatic heart of a girl twenty-two years old.

Cardiac pain and discomfort are well known in rheumatic fever. Gallivardin (1908) reported a case of severe pain in a seven-year-old child, and seems to have attributed the trouble to myocardial scars. Kahn (1926) laid great emphasis on infectious diseases and rheumatic fever and reported that of 82 cases of angina, 24 patients had a history of frequent tonsillitis and 20 of rheumatic fever. White and Mudd (1927) reported 8 cases of angina in patients from seventeen to twenty-six years of age, all of whom had rheumatic hearts and aortic insuf-

ficiency. Stolkind (1928) reported one patient, thirteen years old, who had angina, rheumatic heart disease and aortic insufficiency. He also reported 12 cases from the literature in patients from seven to fourteen years of age, of whom only 2 are shown to have had aortic insufficiency. It is unfortunate that only a few of the cases reported by White and Mudd and by Stolkind came to autopsy. White and Jones (1928) found a history of rheumatic fever in 7 of their 77 cases of angina in adults. Swift and Hitchcock (1928) did not think the pain to be due to coronary or aortic disease in the ordinary sense, but rather to perivascular and adventitial lesions as foci of irritation.

It can be said that while proved coronary thrombosis is rare in rheumatic fever, this is not true of cardiac pain. If cardiac pain be analyzed as it occurs in all age groups, rheumatic fever appears to play a small part, except in such reports as that of Kahn. If, however, it be considered in young patients, rheumatic fever is a common association of the cardiac pain. Certainly many of these patients show aortic insufficiency, but this is not true of all, and even in those with aortic valve involvement the coronary twigs have not been regularly studied. Disease of these twigs is undoubtedly frequent, as we shall demonstrate in this paper, and it is also possible that adventitial and perivascular lesions may well cause interference with the blood supply to the myocardium. Thus it must be accepted that cardiac ischemia cannot be excluded as the cause of the cardiac pain of rheumatic heart disease.

MATERIAL AND METHOD

For this study, 56 hearts were selected from the recent autopsy material of Lakeside Hospital, Babies' and Children's Hospital and Cleveland City Hospital. Only hearts which showed Aschoff nodules or typical rheumatic inflammation were included. Several hearts, ordinarily acceptable as rheumatic, were excluded because Aschoff nodules were not found, even though they showed definite valvular disease. Otherwise the hearts were taken in order as they occurred in the regular autopsy series, and were in no way selected because they showed vascular lesions. Of the 56 patients, 48 gave a history of rheumatic fever, except one who had chorea. There were 15 patients in the first decade, 12 each in the second and third, 10 in the fourth, and 7 in subsequent decades. There were 26 males and 30 females, 44 whites and 12 colored. Forty nonrheumatic hearts were examined as controls, but in many of these infections were present somewhere in the body. The histological material was fixed in neutral formalin, embedded in paraffin, cut at 5 to 7 micra, and routinely stained with hematoxylin and eosin. Special stains included the Verhoeff elastica method, Mallory's connective tissue stain, van Gieson-hematoxylin, Masson trichrome with light green, scarlet R, and for chromotropic substance heavy staining with hematoxylin or

staining with thionin or polychrome methylene blue. The special methods were not used routinely but were employed frequently to clarify features indicated in the hematoxylin and eosin stains.

The observations were recorded on a chart for each heart, and Table I is a summary of the first decade, which illustrates the method for each heart.

RESULTS

First Decade.—The details are to be found in Tables I and II. The lesion observed in the pulmonary arteries was principally in the form of pitting of the intima above the pulmonic orifice. Post-mortem blood cultures were negative in 9 cases, in one yielded *B. coli* and an unidentified streptococcus, and in another streptococcus gamma.

TABLE I

DATA ON RHEUMATIC CORONARIES, FIRST DECADE

Evidence of Rheumatic Fever

Clinical 12; Aschoff nodules 15; rheumatic inflammation 12.
Valve lesions: acute only 2; chronic only 4; both 9.
Coronaries 2; pulmonaries 7; aorta 6.
No note coronaries 3; pulmonaries 2; aorta 2.

Main Coronaries (None in sections 2)

Adventitia: Aschoff 5; fibrosis 6; other cells 6.
Media: edema 13; chromotropic 4; cells 2; fibrosis 4.
Intima: edema 10; chromotropic 4; cells 1; fibrosis 11.
Elastica interna: splitting 9; fragmentation 10; swelling 10.
Other elastica: fragmentation 3; swelling 3.
Thrombosis –; *Fibrinoid:* intima 5; media 4.

Medium-Sized Coronaries

Adventitia: Aschoff 7; fibrosis 8; other cells 6.
Media: edema 15; chromotropic 5; cells 2; fibrosis 4; necrosis 4.
Intima: edema 7; chromotropic –; cells 1; fibrosis 3.
Elastica interna: splitting 3; fragmentation 6; swelling 5.
Other elastica: fragmentation 1; swelling 1.
Thrombosis –; *Fibrinoid:* intima 2; media 8; adventitia 1.

Small-Sized Coronaries

Adventitia: Aschoff 9; fibrosis 7; other cells 8.
Media: edema 13; chromotropic 3; cells 1; fibrosis 1; necrosis 4.
Intima: edema 7; chromotropic –; cells –; fibrosis 3.
Elastica interna: splitting 1; fragmentation 3; swelling 1.
Other elastica: fragmentation –; swelling –.
Thrombosis 2; *Fibrinoid:* intima 2; media 5; adventitia 3.

In summary, the coronary tree in parts showed edema in all cases, associated with fibrinoid in all, and with chromotropic change in 7 cases. Necrosis was observed in 6 cases. Inflammatory reaction as shown by lymphocytes, plasma cells, endothelial cells and sometimes polymorphonu-

clears was found in the adventitia in 9 cases and in other coats in 5 cases. The Aschoff nodules were found in the adventitia in 11 cases and in the media in one case. Elastica changes were observed in all but 2 cases, in both of which adventitial inflammation was observed, in one with medial necrosis and in the other associated with inflammation and thrombosis of veins. Fibrosis of the adventitia was observed in 10 cases, of the media in 5 cases, and of the intima in 12 cases. Degenerative changes were found in all cases and in all were associated with either inflammation or fibrosis, or both. In 3 cases the various types of lesion were not all present. In a colored female two and one-half years

TABLE II

FIRST DECADE—CORONARY LESIONS

	COLOR	SEX	AGE (YEARS)	EDEMA	CHROMOTROPIC	FIBRINOID	NECROSIS	ELASTICA ALTERATIONS	ASCHOFF NODULES		INFLAMMATIONS			FIBROSIS			GROSS SCLEROSIS
									ADVENTITIA	MEDIA	ADVENTITIA	MEDIA	THROMBOSIS	DVENTITIA	MEDIA	INTIMA	
3985	B.	F.	2½	+	−	+	−	+	−	−	−	−	A	−	−	+	+
8690	B.	M.	4⅓	+	+	+	+	+	+	−	+	−	−	+	+	+	−
8687	B.	M.	5	+	+	+	+	+	+	−	+	−	−	+	+	+	−
3585	B.	F.	5	+	+	+	+	+	+	−	+	−	V	+	−	−	−
3999	W.	F.	6	+	−	+	−	+	+	+	+	−	V	−	−	−	−
4229	W.	F.	7	+	+	+	−	+	+	−	+	−	A	+	+	+	−
183	B.	M.	7	+	−	+	−	−	−	−	+	−	V	−	−	−	0
2	B.	M.	7	+	−	+	+	+	+	−	+	−	−	+	−	−	−
3782	W.	F.	7	+	+	+	+	+	−	−	+	−	−	+	−	+	0
377	W.	F.	7	+	+	+	−	+	−	−	−	−	−	+	−	+	+
3685	W.	M.	8	+	+	+	+	+	+	−	+	+	−	+	−	+	−
3923	W.	F.	8	+	−	+	−	+	−	−	−	−	−	−	−	+	−
3800	W.	F.	8	+	−	+	−	+	+	−	+	+	V	+	−	+	−
283	W.	F.	9	+	+	+	−	+	+	−	−	+	−	+	−	+	0
3819	W.	F.	10	+	+	+	−	+	+	−	+	+	V	+	+	+	−

In all tables: + means present. − means absent. 0 means no note in protocol. V means vein. A means artery. C means capillary.

old, degeneration appeared to be the principal lesion, but it was accompanied by gross intimal fibrosis of the coronaries, more widespread microscopically, and definite swelling of the elastica. In a colored male seven years old the arterial lesion, in addition to degeneration, was only inflammation in the adventitia, but the veins showed edema, inflammation of adventitia and thrombosis. In another colored male seven years old the arterial degeneration was accompanied by actual medial necrosis and adventitial inflammation. If these cases be regarded as showing only slight arterial disease, 13 of the 15 cases showed significant disease in various parts of the coronary arterial tree.

TABLE III

DATA ON RHEUMATIC CORONARIES—SECOND DECADE

Evidence of Rheumatic Fever

Clinical 10; Aschoff nodules 12; rheumatic inflammation 10.

Valve lesions: Acute only 1; chronic only 1; both 9.

Coronaries 4; pulmonaries 2; aorta 7.

No note: coronaries 5; pulmonaries 3; aorta 1.

Main Coronaries (None in sections 2)

Adventitia: Aschoff −; fibrosis 3; other cells 5.

Media: edema 10; chromotropic 2; cells −; fibrosis 3; necrosis 1.

Intima: edema 10; chromatropic 1; cells 1; fibrosis 10.

Elastica interna: splitting 7; fragmentation 7; swelling 8.

Other elastica: fragmentation 3; swelling 1.

Thrombosis −; *Fibrinoid:* intima 5; media 8.

Medium-Sized Coronaries

Adventitia: Aschoff 4; fibrosis 6; other cells 5.

Media: edema 11; chromotropic 1; cells −; fibrosis 1; necrosis 4.

Intima: edema 7; chromotropic 1; cells −; fibrosis 7.

Elastica interna: splitting 2; fragmentation 4; swelling 5.

Other elastica: fragmentation −; swelling −.

Thrombosis −; *Fibrinoid:* intima 3; media 9.

Small-Sized Coronaries

Adventitia: Aschoff 9; fibrosis 4; other cells 4.

Media: edema 10; chromotropic −; cells 1; fibrosis 3; necrosis 4.

Intima: edema 3; chromotropic −; cells −; fibrosis 4.

Elastica interna: splitting 1; fragmentation 3; swelling 1.

Other elastica: fragmentation −; swelling −.

Thrombosis −; *Fibrinoid:* intima 3; media 9; adventitia 1.

TABLE IV

SECOND DECADE—CORONARY LESIONS

	COLOR	SEX	AGE (YEARS)	EDEMA	CHROMOTROPIC	FIBRINOID	NECROSIS	ELASTICA ALTERATIONS	ASCHOFF NODULES: ADVENTITIA	ASCHOFF NODULES: MEDIA	INFLAMMATIONS: ADVENTITIA	INFLAMMATIONS: MEDIA	INFLAMMATIONS: THROMBOSIS	FIBROSIS: ADVENTITIA	FIBROSIS: MEDIA	FIBROSIS: INTIMA	GROSS SCLEROSIS
4029	W.	M.	12	+	−	+	+	+	+	−	+	−	V	+	−	+	0
4106	B.	M.	12	+	−	+	+	+	+	+	−	−	−	+	−	+	0
3506	W.	F.	12½	+	+	+	+	+	+	−	+	−	V	−	−	+	+
344	B.	F.	13	+	+	+	−	+	+	+	+	−	−	+	+	+	+
427	W.	M.	13	+	−	+	−	+	+	−	−	−	−	−	−	+	0
412	W.	F.	13	+	−	+	−	−	+	−	−	−	C	−	−	−	−
3146	W.	F.	14	+	−	+	+	+	+	−	+	−	−	+	−	+	0
3709	W.	F.	14	+	−	+	−	+	+	−	+	−	V	−	−	+	−
3805	B.	M.	18	+	−	+	−	+	−	−	−	−	−	+	−	+	−
6653	W.	M.	19	+	+	+	+	+	+	+	+	+	V	+	+	+	+
3725	W.	F.	19	+	+	+	+	+	+	−	−	−	−	−	−	+	0
3809	W.	F.	20	+	−	+	−	+	−	−	+	−	A	+	−	+	+

Second Decade.—(See Tables III and IV.) One patient, a white male nineteen years old, died as the result of scarlatina, showed complete heart-block, had a typical rheumatic history and at autopsy typical rheumatic myocarditis without valve lesions, but the post-mortem blood culture showed streptococcus alpha. The main trunk of the pulmonary artery was atherosclerotic in 1 case, normal in 8 and not described in 3. The blood cultures showed no growth in 7 cases, streptococcus alpha in 1, streptococcus beta in 1, streptococcus gamma in 2 and *B. coli* and staphylococcus in 1.

In summary, the coronary tree in parts showed edema in all cases, associated with fibrinoid in all, and with chromotropic change in 3 cases. Necrosis was observed in 5 cases. Inflammatory reaction, as shown by cellular infiltration, was found in the adventitia in 5 cases and in other coats in only 1 case. Aschoff nodules were found in the adventitia in 9 cases but not in other coats. Elastica changes were observed in all but 2 cases, in one of which there was adventitial fibrosis with the presence of Aschoff nodules and in the other adventitial Aschoff nodules. Fibrosis was observed in the adventitia in 6 cases, in the media in 4 cases and in the intima in 11 cases. Degenerative changes were found in all cases and in all were associated with inflammation or fibrosis or both. In one case the additional change was only in the form of Aschoff nodules in the adventitia, but there were no sections of larger arteries, and in another case there were only the additional appearances of Aschoff nodules in the adventitia and intimal fibrosis. If these 2 cases be regarded as showing relatively insignificant arterial disease, 10 of the 12 cases showed significant disease in various parts of the coronary arterial tree.

Third Decade.—(See Tables V and VI.) The pulmonary arteries showed selerosis in 3 cases, were not noted in 4 cases and revealed no change in 5 cases. Post-mortem blood cultures were negative in 4 cases, were not made in 3 cases; in 1 case yielded *Staphylococcus aureus*, in

TABLE V

DATA ON RHEUMATIC CORONARIES—THIRD DECADE

Evidence of Rheumatic Fever

Clinical 11; Aschoff nodules 12; rheumatic inflammation 11.
Valve lesions: acute only 1; chronic only 1; both 10.
Coronaries 3; pulmonaries 3; aorta 8.
No note 3; pulmonaries 4; aorta 1.

Main Coronaries (None in sections 2)

Adventitia: Aschoff 1; fibrosis 2; other cells 8.
Media: edema 9; chromotropic 5; cells –; fibrosis 2.
Intima: edema 8; chromotropic –; cells 1; fibrosis 8.
Elastica interna: splitting 8; fragmentation 9; swelling 8.
Other elastica: fragmentation 2; swelling 1.
Thrombosis 1; *Fibrinoid:* intima 8; media 8.

TABLE V—CONT'D

Medium-Sized Coronaries

Adventitia: Aschoff 3; fibrosis 11; other cells 6.
Media: edema 12; chromotropic 4; cells –; fibrosis 2; necrosis 5.
Intima: edema 5; chromotropic –; cells –; fibrosis 10.
Elastica interna: splitting 4; fragmentation 5; swelling 8.
Other elastica: fragmentation 1; swelling –.
Thrombosis 1; *Fibrinoid:* intima 6; media 8; adventitia 1.

Small-Sized Coronaries

Adventitia: Aschoff 6; fibrosis 11; other cells 7.
Media: edema 12; chromotropic 1; cells –; fibrosis 1; necrosis 7.
Intima: edema 5; chromotropic –; cells –; fibrosis 11.
Elastica interna: splitting 4; fragmentation 2; swelling 8.
Other elastica: fragmentation –; swelling 1.
Thrombosis 2; *Fibrinoid:* intima 7; media 10; adventitia 1.

TABLE VI

THIRD DECADE—CORONARY LESIONS

	COLOR	SEX	AGE (YEARS)	EDEMA	CHROMOTROPIC	FIBRINOID	NECROSIS	ELASTICA ALTERATIONS	ASCHOFF NODULES		INFLAMMATIONS			FIBROSIS			GROSS SCLEROSIS
									ADVENTITIA	MEDIA	ADVENTITIA	MEDIA	THROMBOSIS	ADVENTITIA	MEDIA	INTIMA	
3398	W.	F.	21	++	–	+	–	+	+	–	+	–	A	+	–	+	–
3224	W.	M.	22	++	+	+	–	+	+	–	+	–	–	+	–	+	–
4050	W.	M.	22	++	+	+	+	+	–	–	+	Intima	A	+	–	+	+
6022	W.	M.	23	+	+	+	+	+	+	–	+	–	–	+	+	+	+
3864	B.	M.	24	+	–	+	–	+	+	–	+	–	V	+	–	+	0
3321	W.	M.	25	+	+	+	+	+	+	–	+	–	–	+	+	+	–
2307	W.	M.	26	+	–	+	+	+	+	–	–	–	V	+	–	+	–
3666	W.	M.	26	+	–	+	+	+	–	–	+	–	–	–	–	+	–
3773	W.	M.	26	+	+	+	+	+	–	–	+	–	AV	+	+	+	+
3235	W.	M.	29	+	–	+	+	+	+	–	+	–	–	+	–	+	0
4069	B.	F.	29	+	+	+	+	+	–	–	+	–	V	+	–	+	–
3355	W.	M.	30	+	+	+	+	+	+	–	+	–	–	+	+	+	0

another Gram-positive diplococci, in another streptococcus alpha, another streptococcus beta and another streptococcus gamma.

In summary, edema of some part of the arterial tree was found in all cases, with chromotropic substance in 7. Fibrinoid was observed in all cases and necrosis in 9. All cases showed elastica alterations. Aschoff nodules were found in the adventitia in 8 cases. Inflammation was observed in the adventitia in 11 cases and the intima in 1. Thrombosis in arteries was observed in 3 cases and in veins in 4 cases. Fibrosis was observed in the adventitia in 11 cases, in the media in 4 cases, and in the intima in all cases. In no case was the disease limited to degenera-

Table VII

Data on Rheumatic Coronaries—Fourth Decade

Evidence of Rheumatic Fever

Clinical 10; Aschoff nodules 9; rheumatic inflammation 7.
Valve lesions: acute –; chronic only 4; both 6.
Coronaries 4; pulmonaries 6; aorta 10.
No note: coronaries 4; pulmonaries 2; aorta –.

Main Coronaries (None in sections 2)

Adventitia: Aschoff 1; fibrosis 5; other cells 7.
Media: edema 8; chromotropic 5; cells 2; fibrosis 7; necrosis 1.
Intima: edema 8; chromotropic 2; cells 1; fibrosis 8.
Elastica interna: splitting 8; fragmentation 8; swelling 8.
Other elastica: fragmentation 3; swelling 2.
Thrombosis –; *Fibrinoid:* intima 6; media 6.

Medium-Sized Coronaries

Adventitia: Aschoff 3; fibrosis 10; other cells 7.
Media: edema 10; chromotropic 3; cells –; fibrosis 2; necrosis 9.
Intima: edema 4; chromotropic –; cells –; fibrosis 5.
Elastica interna: splitting 4; fragmentation 7; swelling 9.
Other elastica: fragmentation –; swelling –.
Thrombosis –; *Fibrinoid:* intima –; media 8; adventitia 1.

Small-Sized Coronaries

Adventitia: Aschoff 5; fibrosis 10; other cells 6.
Media: edema 9; chromotropic –; cells –; fibrosis 3; necrosis 8.
Intima: edema 5; chromotropic –; cells –; fibrosis 6.
Elastica interna: splitting 1; fragmentation 6; swelling 6.
Other elastica: fragmentation –; swelling –.
Thrombosis –; *Fibrinoid:* intima 1; media 5.

Table VIII

Fourth Decade—Coronary Lesions

	COLOR	SEX	AGE (YEARS)	EDEMA	CHROMOTROPIC	FIBRINOID	NECROSIS	ELASTICA ALTERATIONS	ASCHOFF NODULES		INFLAMMATIONS			FIBROSIS			GROSS SCLEROSIS
									ADVENTITIA	MEDIA	ADVENTITIA	MEDIA	THROMBOSIS	ADVENTITIA	MEDIA	INTIMA	
4042	W.	M.	32	+	–	+	+	+	+	–	+	–	V	+	+	+	0
3868	W.	F.	35	+	–	+	+	+	+	–	+	+	–	+	+	+	+
8727	W.	M.	37	+	+	+	+	+	–	–	+	–	–	+	+	+	+
3735	W.	F.	38	+	+	+	+	+	+	–	+	–	–	+	+	+	–
3053	W.	F.	39	+	–	+	+	+	+	+	+	+	–	+	+	+	0
4018	W.	F.	39	+	+	+	+	+	–	–	+	–	–	+	–	+	+
3418	W.	F.	39	+	+	+	+	+	–	–	+	–	–	+	–	+	0
3463	B.	F.	39	+	–	+	+	+	+	–	+	–	–	+	–	+	–
4016	W.	M.	39	+	+	+	+	+	–	–	+	–	–	+	+	+	+
3884	W.	M.	40	+	+	+	+	+	–	–	–	–	–	+	+	+	0

tion, and in this decade it can be stated that some part of the coronary arterial tree showed significant lesions in all cases.

Fourth Decade.—(See Tables VII and VIII.) The pulmonary arteries showed sclerosis in 6 cases, were negative in 2 and were not noted in 2. Post-mortem blood cultures were negative in 6 cases, not made in 3 cases and in 1 case yielded pneumococcus type IV.

In summary, edema of some sort of the arterial tree was found in all cases, combined with chromotropic substance in 6. Fibrinoid, necrosis, and elastica alterations were found in all cases. Aschoff nodules were present in the adventitia in 5 cases, invading the media in 1. Inflammation was found in the adventitia of 9 cases, invading the media in 1, the same case in which Aschoff nodule involvement was observed. Thrombosis was found in the veins of one case. Fibrosis of the adventitia was present in all cases, of the media in 7 cases and of the intima in all cases. One case only, a white male forty years old, failed to show inflammatory lesions of the arteries, but the vessels showed all the forms of degenerative lesion as well as fibrosis of all three coats.

Fifth and Subsequent Decades.—(See Tables IX and X.) The pulmonary arteries were sclerotic in 5 cases and negative in 2. Post-mortem blood cultures were negative in 5 cases and were contaminated in 2.

TABLE IX

DATA ON RHEUMATIC CORONARIES—FIFTH AND SUBSEQUENT DECADES

Evidence of Rheumatic Fever

Clinical 5; Aschoff nodules 7; rheumatic inflammation 7.
Valve lesions: acute –; chronic only 2; both 5.
Coronaries 6; pulmonaries 5; aorta 6.
No note: coronaries 1.

Main Coronaries (None in sections 2)

Adventitia: Aschoff –; fibrosis 3; other cells 4.
Media: edema 5; chromotropic 3; cells –; fibrosis 4; necrosis 1.
Intima: edema 5; chromotropic –; cells –; fibrosis 5.
Elastica interna: splitting 4; fragmentation 5; swelling 5.
Other elastica: fragmentation –; swelling –.
Thrombosis –; *Fibrinoid:* intima 3; media 4.

Medium-Sized Coronaries

Adventitia: Aschoff 3; fibrosis 5; other cells 5.
Media: edema 7; chromotropic 2; cells –; fibrosis 3; necrosis 3.
Intima: edema 2; chromotropic 1; cells –; fibrosis 5.
Elastica interna: splitting 2; fragmentation 6; swelling 7.
Other elastica: fragmentation –; swelling –.
Thrombosis 1; *Fibrinoid:* intima 2; media 6.

Small-Sized Coronaries

Adventitia: Aschoff 5; fibrosis 7; other cells 5.
Media: edema 7; chromotropic 2; cells –; fibrosis –; necrosis 6.
Intima: edema 2; chromotropic –; cells –; fibrosis 7.
Elastica interna: splitting 1; fragmentation 4; swelling 5.
Other elastica: fragmentation –; swelling –.
Thrombosis –; *Fibrinoid:* intima 3; media 4; adventitia 2.

TABLE X

FIFTH AND SUBSEQUENT DECADES—CORONARY LESIONS

	COLOR	SEX	AGE (YEARS)	EDEMA	CHROMOTROPIC	FIBRINOID	NECROSIS	ELASTICA ALTERATIONS	ASCHOFF NODULES		INFLAMMATIONS			FIBROSIS			GROSS SCLEROSIS
									ADVENTITIA	MEDIA	ADVENTITIA	MEDIA	THROMBOSIS	ADVENTITIA	MEDIA	INTIMA	
3859	W.	F.	43	+	+	+	+	+	−	−	+	−	−	+	+	+	+
3933	W.	F.	43	+	+	+	+	+	+	−	+	−	−	+	+	+	0
3606	W.	M.	44	+	−	+	+	+	+	−	+	−	−	+	+	+	+
3883	W.	F.	50	+	−	+	+	+	+	−	+	−	−	+	+	+	+
3356	W.	M.	58	+	+	+	+	+	+	−	+	−	−	+	+	+	+
3820	W.	F.	63	+	−	+	+	+	+	−	+	−	A	+	−	+	+
3744	W.	F.	67	+	+	+	+	+	+	−	+	−	−	+	−	+	+

In summary, edema of some part of the arterial tree was present in all cases, with chromotropic substance in 4. Fibrinoid, necrosis, and elastica alterations were found in all cases. Aschoff nodules were found in the adventitia in 6 cases, without invasion of media. Adventitial mononuclear cell infiltration was found in all cases. Arterial thrombosis was found in 1 case. Fibrosis was observed in adventitia and intima of all cases and in the media of 5. All cases showed degenerative and inflammatory lesions and fibrosis.

SUMMARY OF RESULTS

All cases showed edema of some part of the arterial tree. Chromotropic change was found to be about equally frequent in all decades except the second, in which one-third of the cases showed it as compared with about two-thirds in the other decades. Fibrinoid was found in all cases. Necrosis increased in frequency as age advanced. It was observed in 40 per cent of the cases of the first decade, 50 per cent of the second, 75 per cent of the third, and 100 per cent subsequently. Elastica alterations were found in about 90 per cent of the cases in the first 2 decades and in all cases thereafter. Aschoff nodules in the adventitia were somewhat more frequent in the first three decades than in subsequent decades. Their invasion into the media was

PLATE I

Fig. 1.—Edema of media, the so-called "état reticulaire," in a small epicardial coronary artery. Female, aged two and one half years. Hematoxylin and eosin Wratten green filter B-58. ×150.

Fig. 2.—Edema of intima and media in large epicardial vein. Female, aged twenty years. Hematoxylin and eosin. Wratten green filter B-58. ×215.

Fig. 3.—Necrosis in media of small intramural artery, with a small vacuolated area of edema. Male, aged five years. Hematoxylin and eosin. Wratten green filter B-58. ×335.

Fig. 4.—Fibrinoid degeneration in upper media of large coronary artery, with many nodal points. Female, aged thirty-five years. Hematoxylin and eosin. Wratten green filter B-58. ×230.

AM. HEART JOUR.
VOL. 9, NO. 5, JUNE, 1934

Fig. 2.

Fig. 4.

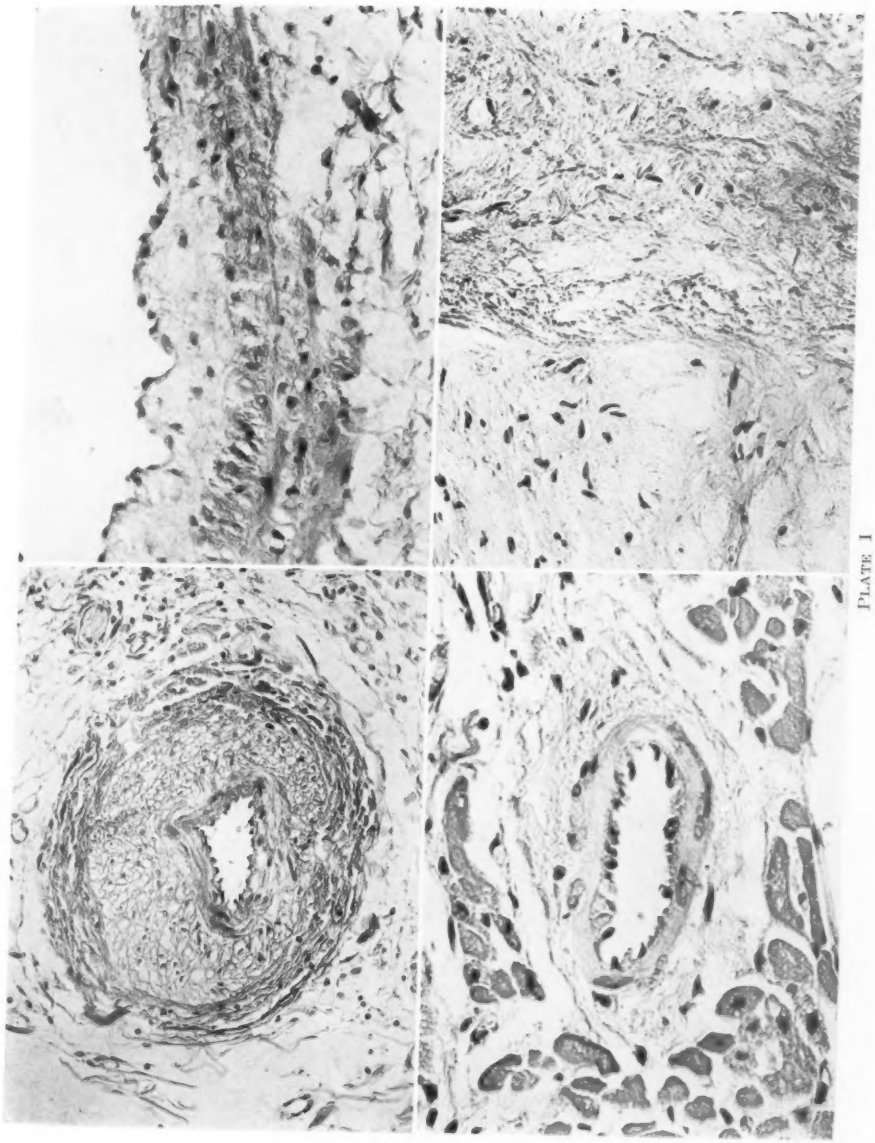


Fig. 1.

Fig. 3.

PLATE I

AM. HEART JOUR.
VOL. 9, NO. 5, JUNE, 1934

PLATE II

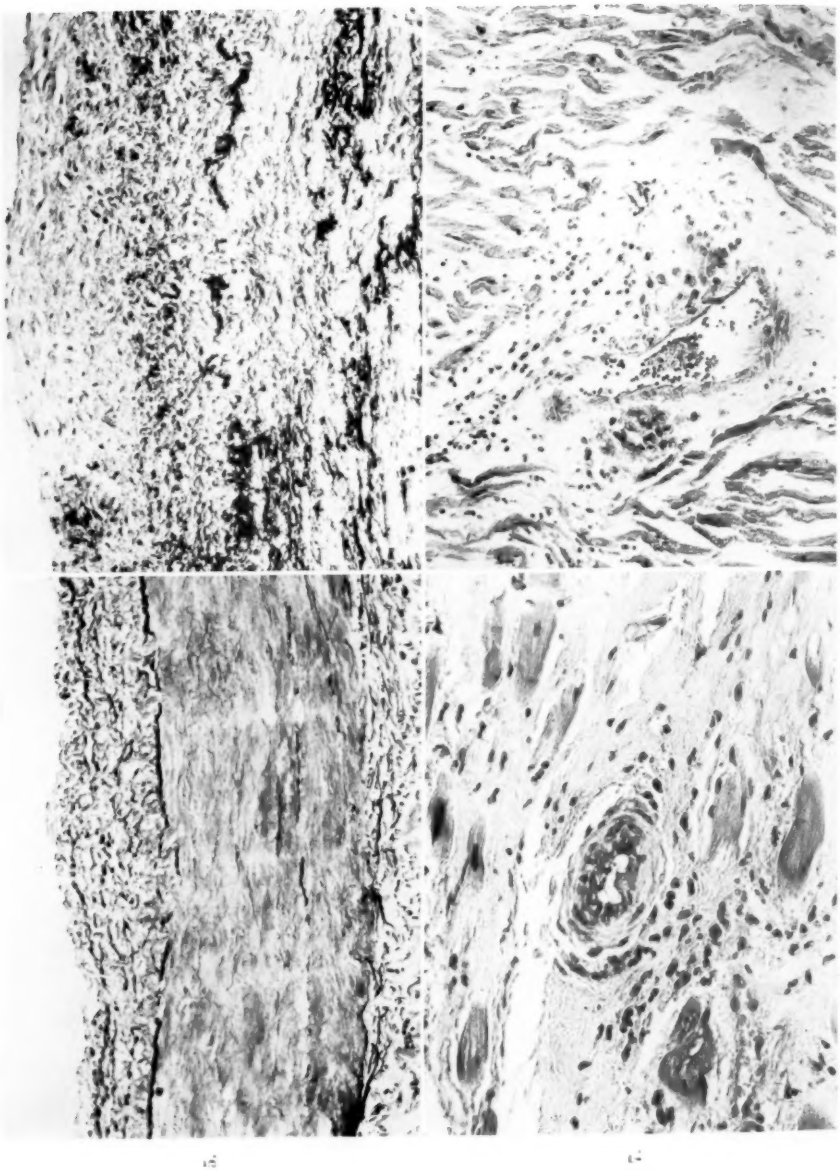


Fig. 6.

Fig. 8.

Fig. 5.

Fig. 7.

more frequent in the first 2 decades than later. Infiltration of mononuclear cells into the adventitia was observed in about two-thirds of the cases of the first 2 decades, about 90 per cent of those of the third and fourth decades, and in all the older cases. Infiltration into the media was present in 27 per cent of the cases of the first decade, 8 per cent of those of the second, 20 per cent of those of the fourth, and in none of those of the third, fifth and subsequent decades. Thrombosis was noted in the smaller arteries in 6 cases, in the capillaries in one case and in the veins in 14 cases, a total of 21 cases or 37 per cent of the series. It was found in about one-half of the cases of the first three decades and in about 10 per cent of those of subsequent decades. Fibrosis of the adventitia was observed in 73 per cent of the cases of the first decade, 58 per cent of those of the second, 92 per cent of those of the third, and all of the cases in later periods. Fibrosis of the media was found in 26 per cent of the cases of the first decade, 17 per cent of those of the second decade, 33 per cent of those of the third, and 70 per cent of those of the fourth and subsequent decades. Fibrosis of the intima was noted in 73 per cent of the cases of the first decade, 92 per cent of those of the second, and all the cases of the third and subsequent decades. Of the cases in which notation was made, grossly observable sclerosis of the coronaries was found in 18 per cent in the first decade, 56 per cent in the second, 33 per cent in the third, 66 per cent in the fourth, and all in the fifth and subsequent decades. Microscopically, severe fibrosis of the intima of the large divisions of the coronaries (when present in the sections) was observed in 38 per cent of the cases of the first decade, 50 per cent of those of the second, 70 per cent of those of the fourth, and all the cases of the subsequent decades. Of 28 patients between the ages of nineteen and forty-four years inclusive, 5 showed sclerosis almost completely occlusive, all males, aged 19, 23, 29, 40 and 44 years respectively.

Thus it is apparent that age has no influence upon edema, chromotropic change, fibrinoid or incidence of Aschoff nodules in the adventitia. As age advances there is an increased incidence of necrosis, elastica alterations, infiltration of mononuclear cells in adventitia, fibrosis of each coat of the arteries and grossly observable sclerosis. The incidence of thrombosis is markedly decreased after the third decade.

Degenerative lesions were found commonly in the controls and are not regarded as significant. In the 56 rheumatic hearts they were ac-

PLATE II

Fig. 5.—Swelling, fragmentation and fraying of elastica in large coronary artery. Female, aged eighteen years. Verhoeff elastica. Wratten orange filter G-15. ×165.

Fig. 6.—Marked swelling and fragmentation of elastica in large coronary artery. Female, aged thirty-two years. Verhoeff elastica. Wratten orange filter G-15. ×165.

Fig. 7.—Marked swelling and wrinkling of elastica in small intramural coronary artery, with apparent reduction of lumen. Male, aged twenty-nine years. Hematoxylin and eosin. Wratten green filter B-58. ×230.

Fig. 8.—Aschoff nodules involving adventitia in a small intramural coronary artery. Male, aged seven years. Hematoxylin and eosin. Wratten green filter B-58. ×140.

companied by acute inflammatory lesions alone in 3 instances, by fibrotic lesions alone in 4 instances, and by both in 49 instances. If both degenerative and inflammatory lesions be excluded, 52 of the 56 hearts showed significant lesions of some part of the coronary tree. The coronaries of two cases, a seven-year-old colored boy and a thirteen-year-old white girl, failed to show elastica alterations, but both these showed inflammatory lesions. Three cases, a seven-year-old white girl, an eight-year-old white girl and a forty-year-old white woman, failed to show inflammatory lesions of the arteries, but all showed intimal fibrosis.

All cases showed intimal fibrosis except 4 in the first decade (all of which exhibited inflammation, and of these 2 showed also venous thrombosis) and one in the second decade which showed Aschoff nodule involvement of adventitia and capillary thrombosis.

Blood cultures showed no apparently significant relation between bacteremia and thrombosis. Of 10 cases from which streptococci were recovered, 5, or 50 per cent, showed thrombosis. Of 31 cases in which the blood culture showed no growth, 11, or 35 per cent, showed thrombosis. Of 12 cases from which organisms other than streptococci were isolated, none showed thrombosis.

DISCUSSION OF RESULTS

In order that the findings might be subjected to further control than that of an extensive experience, the sections from 40 nonrheumatic hearts were examined. These were from patients who had died of infectious disease of short duration, from tumors, poisoning, etc. Definitely cardiovascular cases were excluded. Naturally the tumor patients and those dead of other prolonged disease showed terminal infections. The patients varied in age from eleven months to fifty-eight years. Edema and necrosis of some part of the coronary tree were observed in all cases. Chromotropic substance was not observed. Fibrinoid was found in 18 of the 40 specimens. In the first two decades, comprising 11 cases, elastica change was limited to slight swelling, and the youngest patient to show fragmentation or splitting was twenty-four years old. After that age the more severe elastica lesions were found in 18 of 31 hearts. Fibrosis of the intima was found in only one of the 11 patients

PLATE III

Fig. 9.—Exudative inflammation of medium-sized intramural coronary artery. Female, aged nine years. Adventitia shows fibrosis and polymorphonuclear leucocytes. Media shows fibrosis, edema, infiltration of polymorphonuclears and mononuclears. The intima is destroyed and shows cellular infiltration and marked fibrin formation. There is no organization of the marginal fibrin and the lumen contains erythrocytes. The process reduplicates the endocardial lesion of the same heart. Clinically chorea. Hematoxylin and eosin. Wratten green filter B-58. ×82.

Fig. 10.—Mural fibrin thrombus attached to markedly thickened intima of large coronary artery. Male, aged twenty-four years. Hematoxylin and eosin. Wratten green filter B-58. ×150.

Fig. 11.—Communicating fibrosis of intima and media with distortion of architecture (metallaxis) in large coronary. Female, aged thirteen years. Hematoxylin and eosin. Wratten green filter B-58. ×125.

Fig. 12.—Marked fibrosis of intima with disorganization of media in large coronary. Female, aged ten years. Hematoxylin and eosin. Wratten green filter B-58. ×125.

Fig. 10.

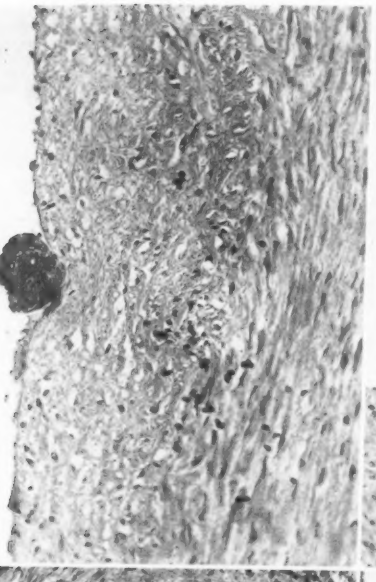
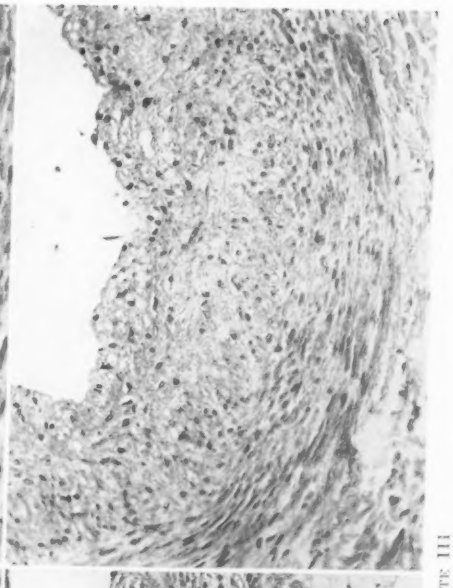


Fig. 12.



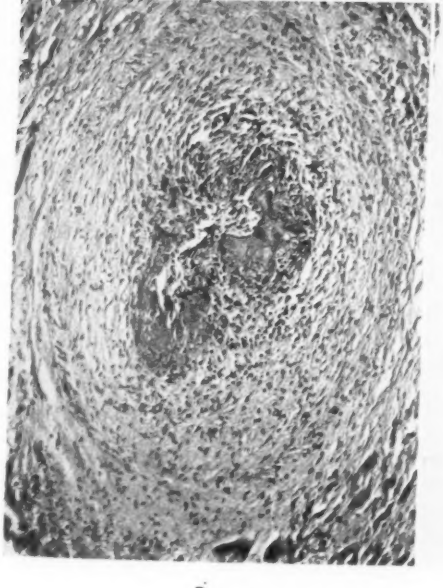


Fig. 9.

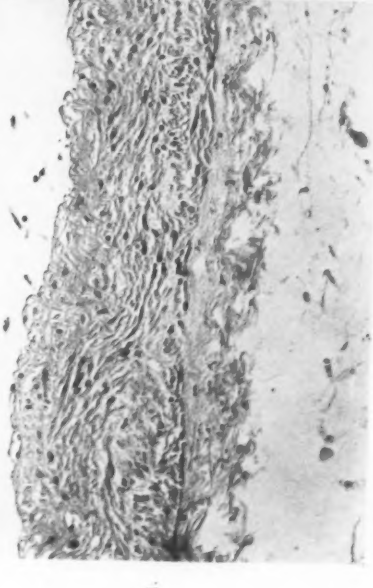


Fig. 11.

PLATE III

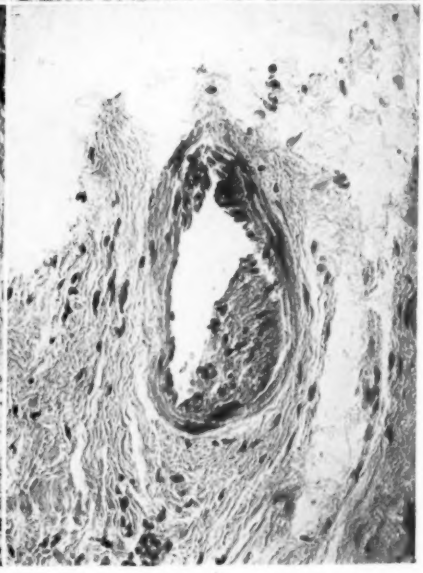
PLATE IV

Fig. 14.

Fig. 16.

Fig. 13.

Fig. 15.



of the first two decades, in two of 10 patients of the third decade, in 6 of 10 of the fourth decade and in 7 of 9 in the fifth decade. Fibrosis of the media was found in 3 of 9 in the fifth decade. Infiltration of mononuclear cells was found in 1 case in the fourth decade. Venous thrombosis was found in only one case, a fifty-eight-year-old white man dead of lobar pneumonia. Gross sclerosis of the coronaries was found in none of the 5 cases of the first two decades where notation was made, in 2 of 5 of the third decade, in 2 of 5 of the fourth decade, in 4 of 5 of the fifth and sixth decades.

Edema is constant in the rheumatic coronaries and in the controls. In both series it is probably due to the presence of infectious disease, circulatory disturbance or both, and is obviously more common in the media than elsewhere. We agree with Segre and Kellner (1921-22) that it is not post-mortem artefact. It is probable that it is in some way related to chromotropic substance. In the control cases chromotropic change was not found in the coronary arteries, but it was observed in more than half of the rheumatic cases. If sections be stained lightly with hematoxylin, it escapes notice and requires heavy hematoxylin staining or staining with polychrome methylene blue or preferably with thionin. These special methods were not used in all cases, and the data here given cannot be regarded as exact. Nevertheless the factor of error is probably much the same throughout, and it seems justifiable to state that chromotropic substance is frequent in the rheumatic coronaries. Cellina (1933) stated that in the aorta chromotropic substance increases as age advances and considered it an age phenomenon rather than the result of pathological change. In our rheumatic coronaries it it almost equally common at all ages. It cannot therefore, in this situation, be an age process alone and is regarded as definitely pathological. That it is more common in rheumatic fever than in other severe infectious diseases is not established by these studies.

The interpretation of exactly what constitutes fibrinoid is not set down by those who have reported on it. For the purpose of this study it has been considered to be an intensely acidophilic substance, arranged in fibrillar fashion sometimes with beading at intersections. It was observed in many of the controls but was found in all the rheumatic cases. It was seen most frequently in the media, but was common in the intima and was found also in the adventitia. There is little doubt as pointed

PLATE IV

Fig. 13.—Marked fibrosis of intima of large coronary artery. Male, aged twenty-four years. Hematoxylin and eosin. Wratten green filter B-58. ×65.

Fig. 14.—Marked intimal sclerosis eccentrically situated in large coronary artery. Male, aged nineteen years. Hematoxylin and eosin. Wratten green filter B-58. ×17.

Fig. 15.—Nodular intimal fibrosis of a small intramural coronary artery. Female, aged fourteen years. Hematoxylin and eosin. Wratten green filter B-58. ×200.

Fig. 16.—Irregular intimal and medial fibrosis with "hyaline scarring" of media in a medium-sized intramural coronary artery. Female, aged forty-three years. Hematoxylin and eosin. Wratten green filter B-58. ×120.

out previously that fibrinoid is most frequent in arteries the seat of the supposedly allergic disturbances, but our control cases and the reports of Henschen (1927) indicate that it may be found in other conditions.

Necrosis was constant in the controls and appeared to be more frequent in the rheumatic series as age increases The control observations nullify those of the rheumatic cases.

Swelling of elastica was frequent in both rheumatic and control cases. Fragmentation and splitting did not occur in the controls until the age of twenty-four years. In the rheumatic cases of the first decade these more severe elastica changes were found in 66 per cent and in the second decade in 58 per cent. Thus it is apparent that severe elastica alterations occur earlier than in the controls. Furthermore the simpler change, swelling, was found to be much more frequent in the rheumatic arteries of the first two decades than in the controls. We have no observations to confirm or contradict the report of Wiesel (1906) that some infections injure the elastica more severely than do others, but can state that rheumatic fever produces early and serious damage to elastica of the coronary arteries.

Aschoff nodules were found to involve the adventitia in about equal percentages at all ages. In the younger individuals they were richly cellular, often with extensive necrosis, but in later life were more fibrous, less frequent in the individual case and often identified with difficulty. In only 4 cases did they extend into the media. We found no evidence that they originate in media. In only rare instances could apparent compression of the vessel be found, but this requires fortunate line of section of a thin-walled artery, and the incidence may be somewhat greater in actual fact than our observations indicate. In no case was complete occlusion by Aschoff nodules observed. The significance of the Aschoff nodules in the arterial walls is that of involvement of the coronary tree in the special type of rheumatic inflammation with the implication of permanent damage. In our opinion the compression of coronary arteries by Aschoff nodules has little if any influence upon the circulation within.

The infiltration into the adventitia of large mononuclear cells, evidently histiocytic in general character, and of those with the morphology of small lymphocytes and plasma cells, was frequent and practically constant after the third decade. This was found in only one of the controls. It is apparently a part of the rheumatic inflammatory reaction and, while not morphologically specific, constitutes part of that picture, drawn by Klinge, of collagenous swelling, fibrinoid degeneration and hyaline scarring to be found in hyperergic reactions. It extended into the media in only 7 cases. Polymorphonuclear leucocytes played only a small part. In 5 cases of the first decade they were found in the adventitia of medium-sized vessels and extended into the intima in one

of these. In one case of the second decade (nineteen-year-old white male) cells were found in the intima of a large coronary, but they could not be positively identified as polymorphonuclear leucocytes. In one case each of the third and fourth decades polymorphonuclear leucocytes were found in the intima of large coronaries. It will probably be necessary to use oxidase stains on suitable material to determine how great a part the polymorphonuclear leucocytes actually play.

The occurrence of ante-mortem blood clots in the vessels has been referred to here as thrombosis. In the smaller vessels it was often occlusive, but in several larger vessels it occurred as a mural lesion. Some were rich in white blood cells, especially leucocytes; others were almost wholly fibrin; and there were mixtures. They occurred both with and without endocarditis lenta. They are interpreted as part of the vascular lesion rather than as emboli. This is in accord with the fact that the controls showed practically no inflammatory lesions of the arteries and in only one case thrombosis. It is not clear that bacteria produce the thrombosis, because in many cases the blood was apparently sterile. The only organisms recovered in cases with thrombosis were streptococci, but in our cases of streptococcemia only half showed thrombosis. That thrombosis is more frequent in rheumatic coronaries than in those of other severe infections is not established.

Although the various forms of intimal disease described by other writers have been observed, attention has been centered on fibrosis. Special stains for fat in numerous instances have demonstrated it in the thickened intima of some of the large coronaries but have been negative in the smaller divisions. Generally the intimal fibrosis in both large and small coronaries has been nodular rather than diffuse. Even in older patients, where extensive fibrosis is often present, it has shown nodular augmentation. Microscopically fibrosis was more often observed in the smaller arteries than in the main stems, and this corresponds to the infrequency of gross sclerosis of the large coronaries in the reports of others and ourselves. By the end of the first decade more than two-thirds of the cases showed under the microscope intimal fibrosis of the smaller vessels. In the second decade 92 per cent exhibited it, and in the third and subsequent decades it was present in all cases. Medial and adventitial fibrosis are more difficult to detect and occur less frequently. The controls showed intimal fibrosis in 1 of 9 cases of the first decade, none in the second, 2 of 10 in the third, 6 of 10 in the fourth and all those of the subsequent decades. Medial and adventitial fibrosis were not found in the controls before the fifth decade. Thus it is apparent that permanent disease appears in the coronary arteries early in the course of rheumatic fever. Our results are in general conformity with those of Zeek (1932) in that gross sclerosis of the coronaries is preco-

cious. Microscopically intimal fibrosis is more frequent than would be indicated by the gross examination.

The nature of the intimal fibrosis is uncertain. The fact that it increases in incidence as age advances indicates that it is progressive and not merely cicatrization or substitution. It is probable that the same is true of rheumatic endocardial and pericardial lesions. Thus the intimal lesions are closely correlated with the other lesions of serous membranes of this disease. Many regard arteriosclerosis in general as of inflammatory character. If this be true, the intimal fibrosis is in the same category.

No evidence was brought out by our observations that regeneration of medial muscle occurs in the course of the arterial disease.

Special attention was not given to the frequency of involvement of arteries other than the coronaries in the rheumatic process, but what have been described as typical lesions in the aorta and pulmonary artery were frequent.

The acute lesions of coronary arteries go hand in hand with acute lesions of the myocardium. The latter are destructive and lead to scarring. The amount of scarring increases with age. This might be thought of as a progressive fibrosis, but with it there are larger and larger areas of muscle destruction, which could hardly be secondary to the fibrosis. Thus the increasing amount of muscle destruction and fibrosis must be due either to recurring acute cycles of rheumatic fever or to chronic arterial disease. Many cases, if the history can be depended upon, are monocyclic. Extensive myocardial fibrosis in these cases can better be explained by chronic arterial disease than otherwise. This leads to the conclusion that the significant arterial lesion for chronic fibrosis of the myocardium is the intimal fibrosis of the smaller branches, a view in accord with that of Brown (1932) as regards myocardial fibrosis in general. Thrombosis can be attributed in most cases either to bacteremia or circulatory failure. When it occurs it is not widespread and neither in the fresh nor cicatrized stage could account for the extensive myocardial fibrosis.

CONCLUSIONS

1. Rheumatic fever regularly produces disease of the coronary arteries. Either inflammatory or fibrotic lesions or both are practically constant. Except for participation by Aschoff nodules, the lesions are not specific for rheumatic fever. Fibrinoid degeneration is suggestive but not diagnostic. Elastica degeneration appears to be especially severe.

2. The coronary disease is irregularly distributed as to both the various divisions of the coronary tree and the individual members affected. Its relation to myocardial disease cannot be positively established, but the late myocardial fibrosis is greater than is to be expected

from the early acute myocarditis alone. The influence of the coronary disease upon myocardial fibrosis is better explained by intimal fibrosis than otherwise.

3. Rheumatic fever predisposes to fibrosis of the coronary arterial tree in early life and to what appears to be precocious coronary sclerosis; but, although this is probably a chronic inflammation, it has not been shown conclusively to be dependent upon the acute degenerative and inflammatory lesions.

4. The coronary arteries in rheumatic fever undergo a progressive sequence of inflammatory lesions which closely resemble those of the endocardium and pericardium. It is practically certain that severe myocardial damage is associated with the arterial disease. The resulting effect upon myocardial efficiency appears to be of significance in the clinical management and prognosis of rheumatic heart disease.

REFERENCES

Apitz, K.: Ueber anaphylaktische Organveränderungen bei Kaninchen, Virchows Arch. f. path. Anat. **289:** 46, 1933.

Idem: Ueber die Gefässwandungschädigung durch Crotalusgift, Centralbl. f. allg. Path. u. path. Anat. **57:** 273, 1933.

Aschoff, L.: Zur Myokarditisfrage, Verhandl. d. deutsch. path. Gesellsch. **8:** 46, 1904.

Idem: Discussion of paper by Lüpke on Periarteriitis nodosa, Verhandl. d. deutsch. path. Gesellsch. **10:** 157, 1906.

Idem, and Tawara, S.: Die heutige Lehre von den pathologisch-anatomischen Grundlagen der Herzschwäche, Jena, 1906, Gustav Fischer.

Astier: Quoted by Rabé.

Barnard, W. G.: Diffuse and Nodular Fibrosis of Adventitia of Aorta (rheumatic periaortitis), J. Path. & Bact. **32:** 95, 1929.

Besançon, F., and Weil, M. P.: La dissociation auriculo-ventriculaire é les arrythmies d'origine rhumatismale, Ann. de méd. **19:** 167, 1926.

Besançon, F., and Weil, M. P.: L'Aortite rhumatismale, Ann. de méd. **19:** 175, 1926.

Bloom, W.: Development of Elastic Fibers in Cultures of Embryonic Heart Muscle, Proc. Soc. Exper. Biol. & Med. **26:** 779, 1929; Studies in Fibers in Tissue Cultures. II. The Development of Elastic Fibers in Cultures of Embryonic Heart and Aorta, Arch. f. exper. Zellforsch. **9:** 6, 1929.

Brown, M.: A Study of the Pathogenesis of Myocardial Fibrosis (''Chronic Fibrous Myocarditis''), Am. J. M. Sc. **184:** 707, 1932.

Breitenecker, L.: Suspected Poisoning; Death From Rheumatic Aortitis, Deutsche Ztschr. f. d. ges. gerichtl. Med. **18:** 312, 1931; Abstract: Arch. Path. **15:** 311, 1933.

Cellina, M.: Sul comportamento della sostanza mucoide dell'aorta negli stati infettiva acuti e cronici, Cuore e circolaz **15:** 506, 1931. Abst.: Centralbl. f. allg. Path. u. path. Anat. **56:** 342, 1933.

Chiari, H.: Ueber Veränderungen in der Adventitia der Aorta und ihrer Hauptäste im Gefolge von Rheumatismus, Beitr. z. path. Anat. u. z. allg. Path. **80:** 336, 1928.

Idem: Ueber Veränderungen in der Arteria pulmonalis in Fällen von akuter rheumatischer Endocarditis oder bei Herzfehler rheumatischen Ursprungs, Klin. Wchnschr. **9:** 1862, 1930.

Idem: Ueber Veränderungen in der Arteria pulmonalis in Fällen von Rheumatismus, Beitr. z. path. Anat. u. z. allg. Path. **88:** 1, 1931.

Coburn, A. F.: Relationship of the Rheumatic Process to the Development of Alterations in Tissues, Am. J. Dis. Child. **45:** 933, 1933.

Cohn, A. E., and Swift, H. F.: Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever, J. Exper. Med. **39:** 1, 1924.

Conner, L. A., and Holt, E.: The Subsequent Course and Prognosis in Coronary Thrombosis, Am. Heart J. **5:** 705, 1930.

Coombs, C.: The Myocardial Lesions of the Rheumatic Infection, Brit. M. J. **2**: 1513, 1907.

Idem: Rheumatic Myocarditis, Quart. J. Med. **2**: 26, 1908-09.

Idem: The Histology of Rheumatic Carditis and Other Rheumatic Phenomena, Brit. M. J. **1**: 620, 1911.

Coombs, C. F.: Rheumatic Heart Disease, New York, 1924, William Wood & Co.

Cowan, J. M.: The Heart in Acute Disease, J. Path. & Bact. **9**: 87, 1904.

Craciun, E. C., Visineanu, N., Gingold, N., and Ursu, A.: Les lésions histologiques de la maladie de Bouillaud. Leur valeur biologique, Ann. d'Anat. Path. **10**: 157, 1933.

Dawson, M. H.: A Comparative Study of Subcutaneous Nodules in Rheumatic Fever and Rheumatoid Arthritis, J. Exper. Med. **57**: 845, 1933.

De Mussy: Quoted by Rabé.

Eiman, J., and Gouley, B. A.: Rheumatic Pneumonitis, Arch. Path. **5**: 558, 1928.

Fahr, T.: Kurze Beiträge zur Frage der Nephrosklerose, Deutsch. Arch. f. klin. Med. **134**: 366, 1920.

Idem: Beiträge zur Frage der Herz- und Gelenkveränderungen bei Gelenkrheumatismus und Scharlach, Virchows Arch. f path. Anat. **232**: 134: 1921.

Idem: Zur Frage der Polymyositis (Dermatomyositis), Arch. f. Dermat. u. Syph. **130**: 1, 1921.

Idem: Vergleichende Herzuntersuchungen bei Scharlach, Streptokokkeninfektion und rheumatischer Granulomatose, Beitr. z. path. Anat. **85**: 445, 1930.

Frothingham, C.: The Relation Between Acute Infectious Diseases and Arterial Lesions, Arch. Int. Med. **8**: 153, 1911.

Gallivardin, L.: A l'étude de la myocardite rhumatismale, à propos d'un fait de myocardite interstitielle avec douleurs précordiales atroces, accès de tachycardie paroxystique et mort rapide sans asystole chez un enfant de 7 ans, Lyon méd. **110**: 753, 1908.

Gastewa, Z. A.: Ueber Arterienveränderungen bei Bauchtyphus, Virchows Arch. f. path. Anat. **289**: 636, 1933.

Geipel, P.: Ueber Myokarditis und Veränderung der quergestreiften Muskeln bei Rheumatismus, München. med. Wchnschr. **56**: 2469, 1909.

Gerstel, G.: Ueber die Veränderungen der Lungenblutgefässe bei Staublungenerkranken, Jena, 1933, Gustav Fisher; Heft 35, Veröffentlichungen aus der Gerwerbe- und Konstitutions-pathologie.

Giraldi, J. J.: The Histology of the Aortic Wall in Acute Rheumatism, Bristol Med.-Chir. J. **46**: 145, 1929.

Gouley, B. A., Bellet, S., and McMillan, T. M.: Tuberculosis of the Myocardium: Report of Six Cases With Observations on Involvement of Coronary Arteries, Arch. Int. Med. **51**: 244, 1933.

Gräff, S.: Pathologische Anatomie und Histologie des Rheumatismus infectiosus, in Rheumaprobleme, Gesammelte Vorträge gehalten auf dem I. Aerztekursus des Rheuma-Forschungs-Instituts am Landesbad der Rheinprovinze in Aachen, Leipzig, 1929, Georg Thieme.

Gray, S. H., and Aitken, L.: Late Gross Lesions in the Aorta and Pulmonary Artery Following Rheumatic Fever, Arch. Path. **8**: 451, 1929.

Gruber, G. B.: Zur pathologischen Anatomie der Periarteriitis nodosa, Virchows Arch. f. path. Anat. **245**: 123, 1923; Zur Frage der Periarteriitis nodosa, mit besonderer Berücksichtigung der Gallenblasen- und Nieren-Beteiligung, Ibid. **258**: 441, 1925.

Hanot, V.: Considerations générales sur le rhumatisme articulaire aigu, Presse méd. **2**: 171, 1894.

Hansmann, G. H., and Schenken, J. R.: Melitensis meningo-encephalitis. Mycotic aneurysm due to Brucella melitensis var. porcine, Am. J. Path. **8**: 435, 1932.

Hayem, G.: Récherches sur les rapports existant entre la mort subite et les altérations vasculaires du coeur dans la fièvre typhoide, Arch. de physiol. norm. et path. **2**: 699, 1869.

Idem: Études sur les myosites symtomatiques, Arch. de physiol. norm. et path. **3**: 422, 473, 569, 1870.

Henschen, F.: Ueber eine eigenartige mit Thrombenbildung verbundene Reaktion des Gefässendothels, Acta. med. Scandinav. **65**: 539, 1927.

Huguenin, P.: Contribution a l'étude de la myocardite infectieuse diphthérique, Rev. de méd. **8**: 790, 995, 1883.

Jäger, E.: Zur pathologischen Anatomie der Thromboangiitis obliterans bei juveniler Extremitätengangrän, Mitt. I. and II, Virchows Arch. f. path. Anat. **284**: 526, 584, 1932.

Idem: Zur histologischen Ausheilung der Periarteriitis nodosa und deren Beziehung zur juvenilen Atheroskierose, Virchows Arch. f. path. Anat. **288**: 833, 1933.

Jores, L.: Arterien, Henke Lubarsch Handbuch der spez. path. Anat. u. Hist., Berlin, 1924, Vol. II, p. 646, Julius Springer.

Kahn, M. H.: Etiologic Factors in Angina Pectoris. An Analysis of Eighty-Two Cases in Private Practice, Am. J. M. Sc. **172**: 195, 1926.

Kerr, W. J., Larkey, S. V., and Larsen, A. E.: Coronary Occlusion and Myocardial Degeneration, California & Western Med. **23**: 46, 1925.

Klinge, F.: Das Gewebsbild des fieberhaften Rheumatismus. I. Mitteilung. Das rheumatische Frühinfiltrat. (Akutes degenerativexsudatives Stadium), Virchows Arch. f. path. Anat. **278**: 438, 1930; II. Mitteilung. Das subakut-chronische Stadium des Zellknötchens, Ibid. **279**: 1, 1931; Der Rheumatismus. Pathologisch-anatomische und experimentell-pathologische Tatsachen und ihre Auswertung für das ärzliche Rheumaproblem, Ergebn. d. allg. Path. u. path. Anat. **27**: 1, 1933.

Idem, and Vaubel, E.: Das Gewebsbild des fieberhaften Rheumatismus. IV. Die Gefässe beim Rheumatismus, insbesondere die "Aortitis rheumatica" (mit Betrachtung zur Aetiologie des fieberhaften Rheumatismus vom pathologisch-anatomischen Standpunkt), Virchows Arch. f. path. Anat. **281**: 701, 1931.

Klinger, H.: Grenzformen der Periarteriitis nodosa, Frank. Ztschr. f. Path. **42**: 455, 1931.

Klotz, O.: Rheumatic Fever and the Arteries, Tr. A. Am. Physicians **27**: 181, 1912.

Idem: Nodular Endarteritis of the Aorta About the Intercostal Arteries, J. M. Research **31**: 409, 1914-15; Fatty Degeneration of the Intima of Arteries, Ibid. **32**: 27, 1915.

Idem: Concerning the Pathology of Some Arterial Diseases, Ann. Int. Med. **4**: 814, 1926.

Idem, and Lloyd, W.: Sclerosis and Occlusion of the Coronary Arteries, Tr. A. Am. Physicians **45**: 108, 1930.

Krehl, L.: Beitrag zur Pathologie der Herzklappenfehler, Deutsch. Arch. f. klin. Med. **46**: 454, 1890.

Krompecher, S.: Telangiostenose, die morphologische Grundlage der "juvenilen" oder "spontanen" Gangränen (Endarteriitis obliterans, Arteriitis obl., Thromboangiitis obl.), Arteriolosclerosis renum und Skleroderma, Beitr. z. path. Anat. u. z. allg. Path. **85**: 647, 1930.

Kugel, M. A., and Epstein, E. Z.: Lesions in the Pulmonary Artery and Valve Associated With Rheumatic Cardiac Disease, Arch. Path. **6**: 247, 1928.

Landouzy, L., and Siredey, A.: Contribution à l'histoire de l'arterite typhoidique, Rev. de méd. **5**: 843, 1885.

Landouzy, L., and Siredey, A.: Étude des localisations angiocardiaques typhoidiques, etc., Rev. de méd. **7**: 804, 919, 1887.

Laubry, C., Huguenin, R., Casteran, R., and Albot, G.: Aortite chronique et myocardite pseudo-gommulaire d'origine vraisemblablement rhumatismale, Ann. d'anat. path. **7**: 614, 1930.

Legroux: Quoted by Rabé.

Levine, S. A., and Brown, C. L.: Coronary Thrombosis: Its Various Clinical Features, Medicine **8**: 245, 1929.

Levy, R. L., and Turner, K. B.: Impaired Auriculoventricular Conduction in Rheumatic Fever, Arch. Int. Med. **43**: 267, 1929.

Lillie, R. D.: Pathology of the Eastern Type of Rocky Mountain Spotted Fever, U. S. Public Health Reports **46**: 2840, 1931 (Reprint No. 1516).

Lisi, F.: Aneurisma metastatico settico dell'arteria epatica, Arch. Ital. di anat. e. istol. pat. **1**: 92, 1930.

Lukomski, P.: Elektrokardiographische Beobachtungen bei akutem Rheumatismus, Deutsches Arch. f. klin. Med. **174**: 268, 1932.

Idem: Elektrokardiographische Beobachtungen bei Abdominaltyphus und Pneumonie, Deutsches Arch. f. klin. Med. **174**: 587, 1933.

MacCallum, W. G.: Rheumatism, J. A. M. A. **84**: 1545, 1925.

Idem: Acute and Chronic Infections as Etiological Factors, Arteriosclerosis. A Survey of the Problem. Publication of the Josiah Macy, Jr., Foundation, edited by E. V. Cowdry, New York, 1933, p. 355, The Macmillan Co.

MacLean, D. L.: Sclerosis of the Coronary Arteries of the Heart, Ann. Int. Med. **2**: 1253, 1929.

Mandelstamm, M.: Ueber die Eigentümlichkeiten der Gefässveränderungen bei sog. chirurgischer Tuberkulose, Virchows Arch. f. path. Anat. **287**: 429, 1932.

Martin, H.: Récheréhes sur la nature et la pathogénie des lésions viscérales consécutives à l'endartérite oblitérante et progressive (scléroses dystrophiques), Rev. de méd. **1**: 369, 1881.

Idem: Récheréhes sur la pathogénie des endocarditis et des scléroses cardiaques. Rev. de méd. **3**: 81, 1883, section on Affections aiguës du coeur d'orgine vasculaire, p. 103.

McClenahan, W. W., and Paul, J. R.: A Review of the Pleural and Pulmonary Lesions in Twenty-Eight Fatal Cases of Active Rheumatic Fever, Arch. Path. **8**: 595, 1929.

McMeans, J. W.: The Splitting of the Elastic Fibers in Arteries, J. M. Research **32**: 377, 1915.

Metz, W.: Die Geweblichen Reaktionserscheinungen an der Gefässwand bei hyperergischen Zuständen und deren Beziehungen zur Periarteriitis nodosa, Beitr. z. path. Anat. u. z. allg. Path. **88**: 17, 1931.

Moritz, A. R.: Medionecrosis Aortae Idiopathica Cystica, Am. J. Path. **8**: 717, 1932.

Oettinger, I., and Neslin, W.: Ueber atrioventrikuläre Automatie bei rheumatischer Karditis, Deutsches Arch. f. klin. Med. **173**: 212, 1932.

Ophüls, W.: Periarteritis Acuta Nodosa, Arch. Int. Med. **32**: 870, 1923.

Pappenheimer, A. M., and Von Glahn, W. C.: Lesions of the Aorta Associated With Acute Rheumatic Fever, and With Chronic Cardiac Disease of Rheumatic Origin, J. M. Research **44**: 489, 1923-24.

Pappenheimer, A. M., and Von Glahn, W. C.: Studies in the Pathology of Rheumatic Fever. Two Cases Presenting Unusual Cardiovascular Lesions, Am. J. Path. **3**: 583, 1927.

Parkinson, J., Gosse, A. H., and Gunson, E. B.: The Heart and Its Rhythm in Acute Rheumatism, Quart. J. Med. **13**: 363, 1919-20.

Paul, J. R.: Pleural and Pulmonary Lesions in Rheumatic Fever, Medicine **7**: 383, 1928.

Perry, C. B.: The Main Branches of the Coronary Arteries in Acute Rheumatic Carditis, Quart. J. Med. **23**: 241, 1929-30.

Rabé, M.: Contribution à l'Étude des lésions des artéres dans l'infection rhumatismale, Presse méd. **10**: 927, 1902.

Ramsey, E. M., and Alpert, L. K.: Response of tissue of the intima to injurious agents, Proc. Soc. Exper. Biol. & Med. **30**: 1433, 1933.

v. Romberg, E.: Ueber die Bedeutung des Herzmuskels für die Symptome und den Verlauf der akuten Endocarditis und der Chronischen Klappenfehler, Deutsches Arch. f. klin. Med. **53**: 141, 1894.

Rössle, R.: Zum Formenkreis der rheumatischen Gewebsveränderungen, mit besonderer Berücksichtigung der rheumatischen Gefässentzündungen, Virchows Arch. f. path. Anat. **288**: 780, 1933.

Sacks, B.: The Pathology of Rheumatic Fever. A Critical Review, AM. HEART J. **1**: 750, 1925-26.

v. Sántha, K.: Ueber Gefässveränderungen im Zentralnervensystem bei Chorea rheumatica, Virchows Arch. f. path. Anat. **287**: 405, 1932.

Scharpf, A.: Ueber das Verhalten der Gefässe bei akuten Infektionskrankheiten, Frank. Ztsch. f. Path. **2**: 391, 1909.

Schenken, J. R., and Hansmann, G. H.: Vascular Lesions of the Gastrointestinal Tract in Mercury Poisoning, Arch. Path. **14**: 152, 1932.

Schultz, A.: Pathologie der Blutgefässe, Lubarsch-Ostertag Ergebn. d. allg. Path. **221**: 207, 1927.

Schulz, M., and Klinge, F.: Das Gewebsbild des fieberhaften Rheumatismus. XIII. Mitteilung. Aortitis rheumatica und Arteriosklerose, Virchows Arch. f. path. Anat. **288**: 717, 1933.

Segre, R., and Kellner, E.: Ueber die sogen. ödematöse Durchtränkung der Arterienwand, Centralbl. f. allg. Path. **32**: 561, 1921-22.

Seifried, O., and Cain, C. B.: Histological Studies of Hog Cholera. II. Lesions of the Vascular System, J. Exper. Med. **56**: 345, 1932.

Semsroth, K., and Koch, R.: Ueber Gefässläsionen bei Allgemeininfektion (Ein Beitrag zur Genese der Periarteriitis nodosa), Krankheitsforschung **8**: 191, 1930.

Siegmund, H.: Ueber nicht syphilitische Aortitis (Pathologisch-Anatomische Demonstration zur Frage der Gefässveränderungen bei Allgemeininfektionen), Ztschr. f. Kreislaufforsch. **21**: 389, 1929.

Slater, S. R.: The Involvement of the Coronary Arteries in Rheumatic Fever, Am. J. M. Sc. **179**: 22, 1930.

Smith, H. L., and Bartels, E. C.: Coronary Thrombosis With Myocardial Infarction and Hypertrophy in Young Persons, J. A. M. A. **98**: 1072, 1932.

Stoerk, O., and Epstein, E.: Ueber arterielle Gefässveränderungen bei Grippe, Frank. Ztschr. f. Path. **23**: 163, 1920.

Stolkind, E. J.: Angina Pectoris in Children, Brit. J. Child. Dis. **25**: 1, 1928.

Sutton, D. C., and Lueth, H.: Diseases of the Coronary Arteries (Myocarditis), St. Louis, 1932, The C. V. Mosby Co.

Swift, H. F.: The Pathogenesis of Rheumatic Fever, J. Exper. Med. **39**: 497, 1924.

Swift, H. F.: The Heart in Infection, AM. HEART J. **3**: 629, 1928.

Swift, H. F., and Hitchcock, C. H.: Cardiac Pain in Rheumatic Fever, J. A. M. A. **90**: 678, 1928.

Swift, H. F., Derick, C. L., and Hitchcock, C. H.: Rheumatic Fever as a Manifestation of Hypersensitiveness (Allergy or Hyperergy) to Streptococci, Tr. A. Am. Physicians **43**: 192, 1928.

Takayasu, R.: Zur Kenntniss der sogenannten Endarteriitis infectiosa und der Knötchenbildung bei rheumatischer maligner Endokarditis, Deutsches Arch. f. klin. Med. **95**: 270, 1909.

Therese: Quoted by Sutton & Lueth.

Von Glahn, W. C., and Pappenheimer, A. M.: Specific Lesions of Peripheral Blood Vessels in Rheumatism, Am. J. Path. **2**: 235, 1926.

Wätjen: Ein besonderer Fall rheumatischer Myokarditis, Verhandl. d. deutsch. path. Gesellsch. **18**: 223, 1921.

Wearn, J. T.: Thrombosis of the Coronary Arteries With Infarction of the Heart, Am. J. M. Sc. **165**: 250, 1923.

White, P. D., and Jones, T. D.: Heart Disease and Disorders in New England, AM. HEART J. **3**: 302, 1928.

White, P. D., and Mudd, S. G.: Angina Pectoris in Young People, AM. HEART J. **3**: 1, 1927.

Wiesel, J.: Ueber Erkrankungen der Koronararterien in Verlaufe akuter Infektionskrankheiten, Wien. klin. Wchnschr. **19**: 723, 1906.

Wiesel, J.: Die "rheumatische" Infektion. I. Die akute Gelenkrheumatismus, Med. Klin. **19**: 163, 1923.

Wiesel, J., and Loewy, R.: Die Erkrankungen der peripheren Gefässe bei akuter und chronischer Kreislaufinsuffizienz, Wien. klin. Wchnschr. **32**: 1083, 1919.

Wiesner, R.: Ueber Veränderungen der Koronargefässe der Infektionskrankheiten, Wien. klin. Wchnschr. **19**: 725, 1906.

Zeek, P.: Studies in Atherosclerosis. II. Atheroma and Its Sequelae in Rheumatic Heart Disease, Am. J. M. Sc. **184**: 356, 1932.

INCIDENCE AND SIGNIFICANCE OF ACTIVE INFECTION IN CASES OF RHEUMATIC CARDIOVALVULAR DISEASE DURING THE VARIOUS AGE PERIODS*†

A Clinical and Pathological Study

M. A. Rothschild, M.D., M. A. Kugel, M.D., and Louis Gross, M.D.
New York, N. Y.

IT IS not an infrequent clinical observation that in cases of rheumatic heart disease the degree of mechanical damage to the heart valves does not necessarily bear a definite relation to the occurrence and extent of heart failure. It was recognized by Krehl as early as 1889 that changes in the myocardium rather than the valvular defect were probably the immediate cause of cardiac failure. In an investigation of ten cases of cardiovalvular disease, chiefly in elderly people, Krehl[1] found fibrosis of the heart muscle, degenerative changes of the coronary arteries and cellular infiltrations in the myocardium. He attributed the diminished functional capacity of the heart to these changes. At this time he expressed the view that systematic studies of the myocardium in cases of valvular disease should be made.

Following the discovery by Aschoff of the specific myocardial lesion in the heart in rheumatic fever, additional attention was directed toward these inflammatory changes in the interpretation of myocardial failure. In general, however, it seems that the opinions expressed along these lines have been based solely on clinical impressions and isolated observations, rather than on an actual careful examination of autopsy material in a large series of cases with a systematic attempt to correlate the anatomical findings with the clinical observations. The present report represents an investigation of the clinical records and autopsy material from 161 cases of rheumatic cardiovalvular disease studied in the Mount Sinai Hospital, in an attempt to determine the incidence of myocardial disease and its relationship to myocardial failure.‡

Because of the uncertainty of clinical data, only those cases were included which presented anatomically and histologically unmistakable evidence of present or past rheumatic heart disease; viz., the presence

*From the Laboratories of the Mount Sinai Hospital, N. Y.

†Aided by a grant from the Lucius N. Littauer Foundation.

‡The terms "heart failure," "circulatory failure" and "myocardial failure" are used interchangeably in this report to indicate congestive failure observed clinically or confirmed by pathological examination. A patient is classified as being in congestive failure even though death may ensue from a complicating condition, such as bronchopneumonia or embolism.

of verrucous endocarditis on a markedly inflamed cusp, Aschoff bodies in the myocardium, the peculiar valvular deformity with its characteristic vascularization, certain types of ring lesions, and an old or recent auricular lesion. These cases were classified as active and quiescent according to the criteria to be described.

CASES WITH ACTIVE INFECTION

Needless to say, the question as to what constitutes activity of rheumatic infection in the heart may be answered quite properly in a number of ways. Grossly, the presence of a fresh pericarditis together with the characteristic verrucous endocarditis is generally considered evidence of activity. Further, the presence in the myocardium of lymphocytes, polymorphonuclear leucocytes, monocytes and swollen or necrotic collagen may be considered as additional signs of activity in a heart showing other unmistakable evidences of rheumatic infection. However, the presence of the Aschoff body in addition to these other findings is accepted as absolute proof of an active rheumatic infection. It is generally agreed not only that the presence of the Aschoff body indicates activity, but also that these lesions can be found in a very high percentage of active cases (Clawson,[2] Thayer,[3] Kugel and Epstein,[4] McClenahan and Paul,[5] and others). In their studies of the standardized sections from rheumatic hearts, Gross, Antopol and Sacks[6] found Aschoff bodies in 90 per cent of 40 hearts showing acute verrucous endocarditis. Thayer found Aschoff bodies in 87.5 per cent of 24 active cases, while McClenahan and Paul found them in 85 per cent of 28 fatal cases of active rheumatic fever.

In our series there were 106 cases which showed anatomical evidence of active infection. Aschoff bodies were found in 95 of these acute cases, an incidence of 89.6 per cent. In the remaining 11 active cases there was present either a fibrinous pericarditis, verrucous endocarditis, acute myocarditis or auricular lesions, but Aschoff bodies were not found after an extensive search.

QUIESCENT CASES

All cases showing the characteristic valvular deformity with or without evidences of old auricular lesions but without the presence histologically of swollen collagen, inflammatory cells, Aschoff bodies or a fibrinous pericarditis were placed in this group.

OUTLINE OF THE PROBLEMS

Having thus outlined our definitions of the type of material we used and our basis for judging of activity and quiescence, we wish to report in this paper first the incidence of quiescence and of active rheumatic myocarditis during the various age periods, and second, the significance of active infection and valvular deformities in their relation to myocardial failure.

With regard to the first problem, it is obvious that our statistics will depend, as do others, on the age of the patients, on the general incidence of the disease in the community from which this hospital draws its material, and on the relative difficulty with which autopsy permits are obtained from the various races which inhabit our wards. The ward service of the Mount Sinai Hospital consists of 500 beds for medical and surgical cases. One hundred of these are set aside for pediatrics. The hospital admits individuals of all ages and of various nationalities. Permission for autopsy examination was granted in a high percentage of cases, on the average 75 per cent in the past seven years. The incidence of autopsy permits was about equal in all age periods and for the various races represented. We may therefore assume that our statistics are a fair representation of the incidence of the disease in general in respect to age periods, bearing in mind the racial peculiarity of our patients and the local incidence of disease in the community.

In a series of 3,000 autopsies there were 180 cases with post-mortem evidence of rheumatic heart disease. As will be indicated in the text, a number of these patients died of conditions other than the past or present rheumatic infection. Complete anatomical investigation was made in 161 of these cases, and our report is based upon the findings in this group. Table I shows the age period incidence of active infection in these cases.

TABLE I

INCIDENCE OF ACTIVE INFECTION IN THE VARIOUS AGE PERIODS

AGE	TOTAL NO. STUDIED	ACTIVE CASES			QUIESCENT CASES		
		NUMBER	PER CENT	NO. DYING IN FAILURE	NUMBER	PER CENT	NO. DYING IN FAILURE
1-10	22	22	100	22	0	0	0
11-20	44	41	95	38	3	5	1
21-30	16	11	78	11	5	22	2
31-40	30	21	70	21	9	30	4
41-50	21	8	38	8	13	62	9
51-60	15	2	13	2	13	87	10
61-70	9	1	12	1	8	88	6
71-80	4	0	0		4	100	3
Total	161	106		103	55		35

CAUSE OF DEATH IN THE VARIOUS DECADES

Twenty-two individuals in this group of 161 cases died in the first decade of life. The youngest was an infant of seventeen months. The myocardium in all these 22 cases showed evidences of activity. In 20, Aschoff bodies were found. All succumbed to myocardial failure. The valvular defects on the whole were minimal. In some instances there was only a slight thickening and rolling of the anterior leaflet of the mitral valve or one of the aortic valve cusps. In three hearts

there was a slight stenosis of the mitral valve. In all these cases the degree of the mechanical defect was so slight that it obviously bore no relationship to the myocardial failure.

In the second decade there were 44 cases. Forty-one of these showed activity in the myocardium. In 37 of these, Aschoff bodies were found. Thirty-eight patients of these cases of acute rheumatic fever with myocarditis died of myocardial failure, or its complications. There were three active cases in which the patients did not die of myocardial failure. One had an extensive pulmonary tuberculosis; another died because of a *Streptococcus hemolyticus* bacteremia; the third died suddenly after an appendectomy, the underlying active rheumatic infection not being recognized clinically. In 35 of the 41 active cases in which the patients died of myocardial failure in which the degree of the valvular defect was studied, nine showed a tight mitral stenosis and two only a moderate valvular stenosis. In the remaining 24, the valvular defect apparently created no great mechanical hindrance to circulation. There were three patients who at the time of death showed no signs of active infection. One patient of these three quiescent cases succumbed to myocardial failure. The valvular defect in this instance was slight. The contributory cause for the myocardial failure was a severe anemia. The patients in the other two quiescent cases succumbed to pneumonia and typhoid fever, respectively.

The number of individuals with rheumatic heart disease dying between twenty and thirty years of age in this series is comparatively small. There were 16 cases, 11 of which showed an active myocarditis. In all of these, Aschoff bodies were found. In all 11 active cases the patients died of myocardial failure. In 3 of these a marked mitral stenosis was present; in 3 others the defect was moderate or slight. There were 5 quiescent cases in this group. Three of these showed no signs of myocardial failure, although in one instance there was a marked stenosis of the mitral and aortic valves. Empyema of the chest *(Streptococcus hemolyticus)*, a postoperative infection and a purulent pneumonia, respectively, caused death in these instances. A fourth quiescent case, a boy of twenty-one years, presenting aortic insufficiency of long duration, gave a history of myocardial failure for seven years. This boy died suddenly, and upon autopsy there was found a well-marked aortic insufficiency and a markedly enlarged heart weighing 1,105 grams. There were no evidences of activity. The fifth quiescent case, a girl of twenty-four years, with mitral stenosis, gave a history of recurrent pulmonary edema associated with mental strain and excitement. She came to the hospital in acute pulmonary edema and at autopsy there were no signs of activity.

The fourth decade group presented some interesting clinical features. It is not uncommon to find individuals at this age without antecedent history of rheumatic infection develop circulatory failure for

the first time, although a well-marked mitral stenosis may be present, indicating that the valvular lesion had existed for a considerable time. The cause for the appearance of circulatory failure at this time is a matter for conjecture; although in several instances an active myocarditis with Aschoff bodies was found on histological examination. There were 30 deaths in this decade. Twenty-one of these 30 cases showed an active myocarditis. In 20 of these, Aschoff bodies were found. In all the cases in the fourth decade showing activity in the myocardium, the patients died of circulatory failure. The extent of the defect and the degree of stenosis of the valves were proportionately greater in this decade. In 12 instances the stenosis was marked, in 4 moderate, and in 4 slight. There were 9 quiescent cases. Four of these patients died of circulatory failure. In one there was coronary artery sclerosis and pulmonary embolism as the terminating cause of death; in another there were multiple pulmonary infarcts and emboli complicating a bronchitis and bronchopneumonia. In the third there was a severe secondary anemia (hemoglobin 18 per cent), while in the fourth case there were found no contributing causes for the myocardial failure. The degree of valvular defect was marked in only one of these. In the remaining 5 quiescent cases the patients died of the following causes: in two instances there was lobar pneumonia, in one a peritonitis, in another a postabortive sepsis, and in the fifth case, a carcinoma of the head of the pancreas. The valvular defects in this latter group were mild.

There were 21 individuals who died in the fifth decade. Eight showed evidence of activity, a surprisingly high incidence so late in life. In 6 of these, Aschoff bodies were found. In all 8 cases with evidence of active infection in the myocardium the patients succumbed to myocardial failure. Thirteen cases were quiescent. Nine of these patients died with evidences of myocardial failure and 4 of other causes. Thus, not only is there a sharp increase in the incidence of quiescent cases in this age period, but there is also an increased incidence in the number of quiescent cases in which the patients died of myocardial failure. A detailed analysis as to the cause of the failure in each quiescent case is of interest. Of the 9 quiescent cases in which the patients died of myocardial failure, hypertension and coronary atherosclerosis played a contributory rôle in 3 instances (two of these cases were further complicated by an occlusion of a coronary artery). Coronary thrombosis was the cause of death in a fourth case, while bronchopneumonia and pleurisy were present in a fifth case. The 4 remaining quiescent cases with evidences of congestive failure were terminated by bronchopneumonia in two instances and by cerebral emboli in the other two. The cause of death in the 4 quiescent cases in which the patients did not die in circulatory failure was as follows: carcinoma in two instances, acute

yellow atrophy in one, and renal and miliary tuberculosis in the other. There was no appreciable difference in the degree of mechanical defect in these groups.

Between the ages of fifty and sixty years there were 15 individuals who presented at necropsy evidence of rheumatic cardiovalvular disease past or present. In two of these, an active myocarditis with Aschoff bodies was found. In one of the active cases the patient died of a lobar pneumonia with some congestive failure, the other succumbed primarily to myocardial failure. In this latter instance, a man of fifty-one with a history of hypertension, there was found at autopsy a marked atherosclerosis of the coronary arteries with some evidence of an old occlusion. Ten patients of the 13 quiescent cases died of myocardial failure. Four of these showed emphysema complicated by chronic bronchitis, pulmonary infarction or coronary artery atherosclerosis. A long-standing hypertension with atherosclerosis of the coronary arteries was the contributing cause of failure in a fifth case, while in a sixth there was in addition a thrombosis of the left anterior descending coronary branch. In the two other quiescent cases in which the patients died of myocardial failure there was a marked aortic stenosis. Death occurred suddenly in both instances. One of these showed diffuse myocardial fibrosis and atherosclerosis of the coronary vessels. The ninth patient, a woman of fifty-three years, died following a cerebral embolism after a month of congestive failure with embolization to the bifurcation of the abdominal aorta. The patient in the tenth quiescent case of death with signs of congestive failure succumbed to a bronchopneumonia following an operation for the removal of an embolus from the brachial artery. There were 3 quiescent cases which presented no evidences of myocardial failure. All three patients died of carcinoma. In 10 of the 15 cases studied, the degree of the valvular defect was determined. In 7 of these there was a marked stenosis of the valves, while in 3 there was only a moderate valvular defect.

Nine individuals with rheumatic cardiovalvular disease survived until the seventh decade. Only one case in this entire group showed evidence of activity with Aschoff bodies in the myocardium. This patient, a woman of sixty-two years, showed in addition evidence of an old occlusion of a coronary artery and recent bronchopneumonia. She died of myocardial failure. Of the 8 quiescent cases, 6 patients had evidences of congestive failure. In two, arteriosclerosis of the coronary arteries was present, in one instance associated with myocardial fibrosis and in the other with hypertension. A third individual, aged sixty-five years, suffered from emphysema and chronic bronchitis and finally developed pneumonia. Three others, women of from sixty-five to sixty-seven years of age, showed some evidences of congestive failure but died of pneumonia complicating hypertension in two instances and chronic bronchitis in a third. There were two quiescent cases in which patients died of

causes other than heart failure—one died of erysipelas complicated by a streptococcus sepsis and the other of carcinoma.

There were 4 survivals in the eighth decade. In none of these was there any sign of active infection. The patients died of circulatory failure. In two of these coronary thrombosis was found, and in the third, in addition to infarctions of the lungs, there was found atherosclerosis of the coronary arteries with infarcts in the myocardium. In two cases the valvular defect was moderate; in the third there was a tight mitral stenosis. The oldest patient studied by us was a woman of eighty years with a tight mitral stenosis and a marked aortic stenosis. She died of a mesenteric artery thrombosis with no signs of myocardial failure.

DISCUSSION

The data presented above confirm the belief that neither the degree of myocardial failure nor its onset necessarily bears a relation to the severity of the valvular defect. A search for the inciting cause producing heart failure indicated that in the first five decades of life an active infection in the myocardium was found with significant frequency. Adults with tight mitral stenosis who are admitted to the hospital with circulatory failure and present no history of either symptoms or knowledge of a previous rheumatic infection not infrequently show on histological examination of the myocardium an active myocarditis of recent origin in a high percentage of the cases.

One hundred and six of the 161 cases studied showed active infection (Table I). In the first decade all of the 22 cases showed evidences of active rheumatic infection, in the second decade 95 per cent, in the third 78 per cent, and in the fourth 70 per cent. From the fifth to the eighth decades the percentage, although rapidly decreasing, is still unexpectedly high, ranging from 8 cases out of 21 (38 per cent) in the fifth decade, to 1 case out of 9 in the seventh decade. This indicates a remarkable persistence, or recurrence, of active rheumatic infection perhaps comparable to that seen in tuberculosis and syphilis.

One hundred and three of the 106 patients showing active lesions in the myocardium died of circulatory failure. Even with the most rigid criteria our studies show a striking correlation, if not an actual causal relationship between heart failure and activity. This is true of those patients dying of circulatory failure even as late as in the fifth decade. The relationship of active infection in bringing about a circulatory breakdown has already been recognized by Coombs[7] and by Wilson and Kopel.[8] In studying the significance of the leucocyte count as an index of rheumatic infection in children, Wilson and Kopel observed that a close correlation seemed to exist between the presence of a leucocytosis and a diminished vital capacity measurement in children with rheumatic heart disease. They feel that this further confirms the conception that

cardiac failure in these children is primarily due to infection rather than to mechanical factors. Coombs has expressed the belief that even in adults as late as thirty or forty years of age, the onset of dyspnea or myocardial failure may be traced to an active myocarditis which he frequently observed on microscopic examination in apparently quiescent cases.

While the causal relationship of active myocarditis to circulatory failure is very striking in the first two decades of life, it is not sufficiently appreciated that in cases of rheumatic heart disease in adults of the third, fourth and fifth decades of life a recurrent rheumatic myocarditis rather than the healed mechanical defects may in the majority of instances be the precipitating cause of the circulatory failure.

The clinical picture of the individuals dying of circulatory failure during the first decade did not vary materially from that of the individuals dying in the third and fourth decades, nor did the grade of circulatory failure differ in individuals in the first attack from that of those dying in a recurrent attack.

These observations apply not only to acute circulatory failure but especially to those cases of protracted circulatory failure which defy our usual therapeutic procedures. An individual in the first five decades of life with a chronic valvular defect whose myocardial efficiency is low, who has edema and a temperature varying from 99° to 100° for which no cause can be found, who does not respond to rest, digitalis and diuretics, and in whom no obvious precipitating cause of the myocardial failure can be discovered, should be suspected of having an active rheumatic infection as the underlying cause of his present failure. It is not uncommon to see such patients suddenly regain efficiency, especially when the signs of active infection have subsided, even when all therapeutic measures had previously failed.

On the other hand, it is true that not all individuals dying of circulatory failure showed active infection in the myocardium. As mentioned before, this parallelism of activity and myocardial failure is seen chiefly in those individuals dying in the first five decades of life.

It is equally important to point out that a number of individuals who have had rheumatic heart disease can become completely quiescent, reach the fifth, sixth, seventh and even the eighth decade of life and ultimately die of a totally unrelated disease without having any evidence during life of myocardial failure directly attributable to the mechanical defects of old rheumatic infection. (Table II.)

Absence of activity, which may be interpreted as quiescence or healing, has been found in this series of fatal cases as early as the second decade. Of the 161 cases investigated, 55 were quiescent. Table I shows the increasing percentage of quiescent cases in the later decades. This increasing incidence of quiescent cases occurs sharply in the fifth decade. Of the 55 quiescent cases studied, 35 patients died of myocardial

TABLE II

CAUSE OF DEATH IN CASES SHOWING NO EVIDENCE OF MYOCARDIAL FAILURE

AGE	SEX	ACTIVITY	CAUSE OF DEATH
13	M	Present	Acute otitis media, sigmoid sinus phlebitis, streptococcus sepsis.
15	M	None	Purulent bronchopneumonia.
17	M	None	Typhoid fever, hemorrhagic lobar pneumonia.
19	M	Present	Postoperative death following appendectomy.
19	F	Present	Extensive pulmonary and generalized tuberculosis.
22	F	None	Chronic pneumonia, streptococcus empyema of chest.
26	F	None	Purulent pneumonia.
30	M	None	Postoperative infection and hemorrhage.
34	F	None	Postabortive sepsis.
35	M	None	Peritonitis.
35	M	None	Lobar pneumonia.
37	F	None	Lobar pneumonia.
40	F	None	Carcinoma of pancreas.
48	M	None	Spongioblastoma in brain.
49	M	None	Carcinoma of bladder.
50	M	None	Generalized tuberculosis.
50	F	None	Acute yellow atrophy of liver.
51	M	None	Carcinoma of bladder.
59	F	None	Carcinoma of colon.
60	M	None	Carcinoma of pancreas.
63	M	None	Erysipelas, streptococcus sepsis.
67	F	None	Carcinoma of head of pancreas.
80	F	None	Mesenteric artery thrombosis.

failure or its complications. Twenty-eight of these were individuals older than forty years. The majority of those who died of circulatory failure in the sixth, seventh and eighth decades showed the contributory causes of heart failure to be expected at this age period, such as long-standing hypertension, coronary artery sclerosis, with occlusion at times, and long-standing pulmonary disease which increases the burden of the right heart. Individuals dying purely of the mechanical hindrance to the circulation due to the deformity of the valves were relatively few in number.

SUMMARY AND CONCLUSIONS

A clinical and pathological study of 161 persons dying with evidence of rheumatic heart disease, past or present, has been made in order to correlate chiefly the occurrence of myocardial failure, the degree of the valvular defects, and the presence of myocardial disease.

Of the 161 cases studied, 106 showed evidence of an active infection. One hundred and three patients of these 106 active cases died of circulatory failure. The occurrence of heart failure in the first five decades of life in individuals who have a valvular defect can, in the majority of instances, be attributed to an active infection of the myocardium rather than to the degree of the mechanical defect. It is striking to

note the high grade of mechanical defect existing in individuals living even to the fifth and sixth decade with little or no evidence of congestive failure.

In a few instances complete quiescence of the rheumatic myocarditis was present as early as the second decade of life. The number of the quiescent cases increased considerably in the later age periods. Circulatory failure in the later decades of life in individuals with valvular defects was found in the majority of cases to be precipitated by the expected contributory causes occurring at this time of life, viz., hypertension, either in the systemic or pulmonary circuit, atherosclerosis of the coronary arteries, coronary thrombosis, myocardial degeneration and fibrosis.

REFERENCES

1. Krehl, Ludolf: Beitrag zur Pathologie der Herzklappenfehler, Deutsch. Arch. f. klin. Med. **46**: 454, 1889.
2. Clawson, B. J.: The Aschoff Nodule, Arch. Path. **8**: 664, 1929.
3. Thayer, W. S.: Notes on Acute Rheumatic Disease of the Heart, Bull. Johns Hopkins Hospital **36**: 99, 1925.
4. Kugel, M. A., and Epstein, E. Z.: Lesions in the Pulmonary Artery and Valve Associated With Rheumatic Cardiac Disease, Arch. Path. **6**: 247, 1928.
5. McClenahan, W., and Paul, J. R.: A Review of the Pleural and Pulmonary Lesions in Twenty-Eight Fatal Cases of Active Rheumatic Fever, Arch. Path. **8**: 595, 1929.
6. Gross, Louis, Antopol, Wm., and Sacks, Benjamin: A Standardized Procedure Suggested for Microscopic Studies on the Heart, Arch. Path. **10**: 840, 1930.
7. Coombs, Carey F.: Rheumatic Heart Disease, New York, 1924, William Wood & Company.
8. Wilson, May G., and Kopel, M.: Significance of the Leukocyte Count as an Index of Rheumatic Infection in Children, Am. J. Dis. Child. **32**: 46, 1926.

THE FORM OF THE ELECTROCARDIOGRAM IN EXPERIMENTAL MYOCARDIAL INFARCTION

I. Septal Infarcts and the Origin of the Preliminary Deflections of the Canine Levocardiogram*

Frank N. Wilson, M.D., Ian G. W. Hill, M.B.,† and
Franklin D. Johnston, M.D.
Ann Arbor, Mich.

INTRODUCTION

THIS article is the first of a series in which the changes in the form of the electrocardiogram observed after the ligation of the various subdivisions of the coronary arteries will be described. The experiments were carried out upon large dogs. In this animal the region supplied by the left coronary artery is much larger than that supplied by the right. A few millimeters from its origin the former vessel divides into three branches: the circumflex, the anterior descending, and the septal. The last nourishes a large part of the ventricular septum. When it is ligated, pronounced disturbances in intraventricular or in atrioventricular conduction usually occur. The anterior descending branch usually supplies most of the ventral wall of the left ventricle including the anterior papillary muscle, and those portions of the ventral wall of the right ventricle that lie near the interventricular sulcus. The circumflex branch usually supplies most of the dorsal wall of the left ventricle, including the posterior papillary muscle and the more apical portions of the dorsal wall of the right ventricle. The right coronary artery supplies the more basal portions of the wall of the right ventricle. There are of course numerous variations in the distribution of these vessels and their branches and in the manner in which they anastomose, so that the extent and the exact location of the infarct produced by ligating any one of them are variable.

The chief purpose of this paper is to describe and to discuss the three experiments in which the septal artery was ligated. In all of these complete right bundle-branch block developed, and we have therefore included here a description of the changes in the form of the levocardiogram observed after the ligation of other coronary arteries.

EXPERIMENTAL PROCEDURE

When we desired to study the immediate effects of coronary ligation, the animal was fully anesthetized with morphine and urethane and brought to the electrocardio-

*From the Department of Internal Medicine, University of Michigan Medical School.
†Of the Department of Medicine, University of Aberdeen.

graphic laboratory, where it was placed upon its back on a dog board. After beginning artificial respiration, the chest was opened by splitting the sternum. An incision parallel to the long axis of the heart was then made in the pericardium, and the cut edges were sewn to the margins of the chest wound so that the heart lay suspended as in a hammock. If the morphine given caused a pronounced slowing of the heart or a tendency to independent ventricular activity, the vagi were cut. For the standard electrocardiographic leads the electrodes were small copper disks with binding posts attached; these were sewn under the skin of the extremities. Similar electrodes were used for precordial leads, which were taken before the chest was opened.

When it was desired to study the late effects of infarction, the ligation operation was done in the surgical laboratories, and morphine and ether were used to induce anesthesia. A flap of skin and muscle in the precordial region was turned back, and the chest was opened by cutting through an intercostal space and retracting the adjacent ribs. A small incision in the pericardium gave access to the vessel selected. After this was tied, the chest was quickly closed layer by layer, and the animal was allowed to recover. Aseptic precautions were observed and infection was rare. No electrocardiograms were taken prior to, or immediately following, the operation. In making electrocardiographic observations after the desired interval had elapsed, the same plan was followed as in the experiments in which the immediate effects of coronary ligation were under investigation.

In ligating the septal artery we adopted the method employed by Lauterbach.[1] A complete description of this method and of the anatomical relations will be found in his article. This vessel is rather difficult to reach; it comes from the under side of the main trunk or the anterior descending branch of the left coronary artery very close to the junction of the anterior descending and circumflex branches. This junction is exposed by careful blunt dissection beneath the left auricular appendage in the angle between the attachment of this appendage and the pulmonary artery. A ligature is then passed first beneath the anterior descending branch close to its origin and then beneath the main trunk and beneath the circumflex branch in turn. When tied it is almost certain to catch the septal vessel. The dissection must be carried out with great care if uncontrollable hemorrhage is to be avoided.

DESCRIPTION OF SEPTAL EXPERIMENTS

The immediate effects of septal ligation were studied in only one animal (Experiment J). In less than two minutes after tying the ligature there was a slight elevation of the RS-T segment of the ventricular complex in Lead I and a pronounced depression of this segment in Lead III. These changes became slightly more conspicuous within the next few minutes (Fig. 1) and persisted. The first evidence of intraventricular block appeared one hour and forty-five minutes after the ligature was tied. At this time incomplete right bundle-branch block developed. Complexes characteristic of complete right branch block were observed about twenty minutes later. After a short period during which the block was at times incomplete no further change in the form of the electrocardiogram occurred. The animal was killed by inducing ventricular fibrillation about four hours after the septal artery was occluded. On opening the heart the infarct was faintly visible as a slightly discolored area, some 3 cm. in diameter, on the left side of the upper

septum. On palpation it was much firmer than the rest of the ventricular muscle. Both of the main subdivisions of the left bundle-branch crossed the affected area, which extended downward to the apex of the posterior papillary muscle and involved the upper three-fifths of the septal muscle. On the right side of the septum no change in the muscle was visible to the naked eye. Microscopic examination of the upper septum showed cloudy swelling and Zenker's necrosis, but no leucocytic infiltration or hemorrhage. No attempt to determine the condition of the bundle branches by histological examination was made in this or in our other experiments.

In two experiments the late effects of septal ligation were studied. In both of these the electrocardiographic observations were made forty-eight hours after tying the artery. In the first (Experiment 46) the

Fig. 1.—Experiment J. Lead I (above) and Lead III taken simultaneously just before and at various intervals after ligation of the septal branch of the left coronary artery. *A* was taken seven minutes before; *B*, three minutes after; *C*, forty-two minutes after; *D*, sixty-two minutes after; and *E*, two hours after tying this vessel.

standard leads taken before opening the chest showed complete right branch block, with ventricular complexes of unusual outline in Leads II and III (Fig. 2). A series of precordial leads was also taken. The exploring electrodes were sewn beneath the skin along a line passing across the precordium in a right-to-left and base-apex direction. This line intersected the midline 15.5 cm. below the episternal notch, and made an angle of about sixty-five degrees with the long axis of the body. The indifferent point paired with each exploring electrode in turn was a central terminal connected to the two fore legs and the left hind leg through resistances of 5,000 ohms.[2] In the curve taken farthest to the right the chief upstroke of QRS is late. It begins about 0.06 second after the first ventricular deflection in Lead I. In the curves from

the left side of the precordium the chief upstroke is early. It occurs about 0.02 second after the first deflection in Lead I. In these curves there is a conspicuous inverted peak synchronous with R in Lead I and a broad upward movement synchronous with S in Lead I. The midline curve is transitional in form, but the main upstroke is early. The precordial electrocardiograms are strikingly similar to those obtained in an

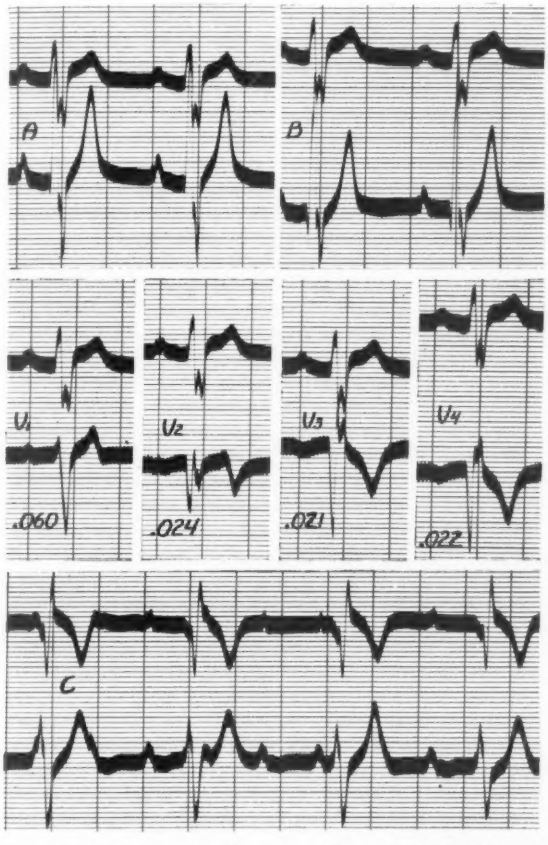


Fig. 2.—Experiment 46. Electrocardiograms taken forty-eight hours after ligation of the septal artery. *A*, Lead I (above) and Lead II; *B*, Lead I and Lead III. The second row shows four precordial leads taken simultaneously with Lead I. In the precordial curves 1 cm. equals 2 millivolts. The indifferent point paired with each exploring electrode was a central terminal (see text). The position of the different exploring electrodes was as follows: V_1, 6 cm. to the right of the midline; V_2, in the midline; V_3, 6.25 cm. to the left of the midline; V_4, 11.5 cm. to the left of the midline. The figures written on the records give the time (in seconds) of the chief upstroke with reference to the beginning of the QRS interval. *C*, Lead I and Lead III taken after opening the chest. Complete heart block is present.

experiment previously reported[3] in which the right branch of the His bundle was cut.

After the precordial leads had been taken, the chest was opened; but before the heart could be exposed, complete atrioventricular block developed. It persisted to the end of the experiment, and direct curves

which could be compared with those taken from the precordium were not therefore obtained. The idioventricular complexes were extremely variable in form, and although direct leads were taken it was not possible to determine with certainty where the ventricular center or centers responsible for the various types of complexes were located. When the ventricular complexes were of the kind shown in Fig. 2, it was thought that the ventricular rhythm arose on the left side. A sharp electrode, insulated except at the tip, failed to yield deflections of the monophasic type when it was thrust through the wall of the right ventricle into the septal muscle, indicating that this muscle, or much of it, was dead.

A photograph of the left side of the septum showing the location of the infarct is shown in Fig. 3. The right side of the septum showed

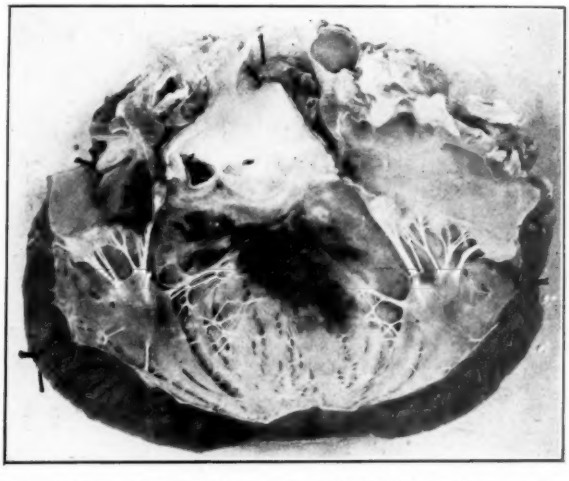


Fig. 3.—Experiment 46. Photograph of the endocardial surface of the left ventricle.

extensive changes of a similar kind, affecting its upper two-thirds. When the septum was sectioned, a large cavity due to liquefaction necrosis was found extending about 1.5 cm. downward from the upper margin. On microscopic examination this cavity was seen to be surrounded by a zone of dense leucocytic infiltration in necrotic muscle. Outside this zone there was an extensive area of patchy necrosis.

In the other instance (Experiment 51) in which the septal artery was ligated, the standard leads showed complete right branch block with ventricular complexes not strikingly different from those usually obtained after the right branch of the His bundle has been cut (Fig. 4). The form of these complexes was considerably altered by opening the chest, but remained the same in general outline. The precordial curves are somewhat distorted by alternating current. The exploring electrodes were sewn beneath the skin along a line which crossed the precordium

in a base-apex direction and intersected the midline at an angle of about seventy-eight degrees 17 cm. below the episternal notch. In the curve taken farthest to the right the chief upstroke of QRS begins about 0.04 second after the beginning of the QRS interval. In that taken furthest to the left the chief upstroke of QRS occurs about 0.02 second after the beginning of the QRS interval. In form the precordial

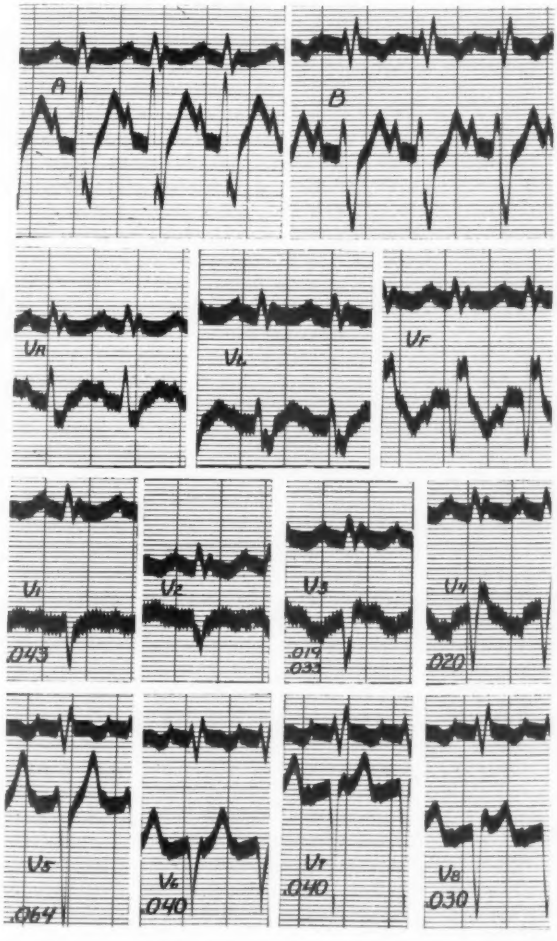


Fig. 4.—Experiment 51. Electrocardiograms taken forty-eight hours after ligation of the septal artery. *A*, Lead I (above) and Lead III before, and *B*, the same leads after opening the chest. V_R, the potential of the right fore leg. V_L, the potential of the left fore leg. V_F, the potential of the left hind leg. Third row shows four precordial curves taken simultaneously with Lead I by the same method as the corresponding curves of Fig. 2 except that here 1 cm. equals 1 millivolt. The position of the various exploring electrodes was as follows: V_1, 6.5 cm. to the right of the midline; V_2, in the midline; V_3, 9.5 cm. to the left of the midline; V_4, 17.5 cm. to the left of the midline. The last row shows a series of leads taken from a gauze pad soaked in saline and laid upon the exposed heart. In these curves 1.5 cm. equals 10 millivolts. The exploring electrode was moved 1.5 to 2 cm. per step in a base-apex direction. V_5 was taken from that part of the pad that lay on the base of the right ventricle and V_8 from that part that lay on the apex of the left ventricle. The indifferent point for these leads was the same as for the precordial leads. The time of the chief upstroke with reference to the beginning of the QRS intervals is written on the records in ink.

curves are similar to the corresponding curves of the previous experiment. The indifferent point was again a central terminal connected to the two fore legs and the left hind leg through resistances of 5,000 ohms. Leads from the first three precordial electrodes were, however, also taken by placing the indifferent electrode on the left hind leg. Usually the precordial curves taken by the two methods show only minor differences, but in this instance the curves taken by the second method are very different from those obtained by the first and are so strikingly alike in form that it is clear that they are dominated by the potential of the hind leg electrode (Fig. 5). The potential variations of this electrode and of the electrodes on the two fore legs were recorded by the method described in a preceding article.[2] The curve from the left hind leg is very much like those from the left side of the precordium (Fig. 4).

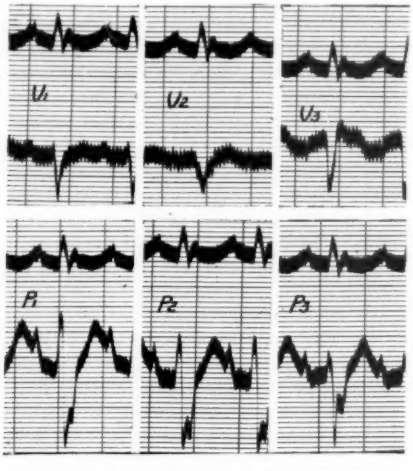


Fig. 5.—Experiment 51. The upper records are the same as V_1, V_2 and V_3 of Fig. 4. The lower records were taken from the same exploring electrodes, but these were paired with the left hind leg electrode instead of with the central terminal.

The curves from the two fore legs are very much alike and are somewhat similar to those from the right side of the precordium (Fig. 4). Semidirect leads from a pad soaked in saline and laid upon the exposed heart were also taken, using the central terminal as the indifferent point. As in the case of the precordial leads, the curve taken farthest to the right shows a late, and that taken farthest to the left an early, chief upstroke. The pad curves and the corresponding precordial curves are similar in general outline (Fig. 4).

Before direct leads could be taken, the heart dilated and the animal died. Photographs of the right and left sides of the septum are reproduced in Fig. 6. On the left side the apex of the anterior papillary muscle was infarcted; this part of the lesion is apparently due to the

unintentional obstruction of a small artery on the left margin of the heart at the time of the ligation operation. Practically the whole of the upper septum was necrotic; on microscopic examination there was a small area of autolytic softening surrounded by a heavy zone of leucocytic infiltration.

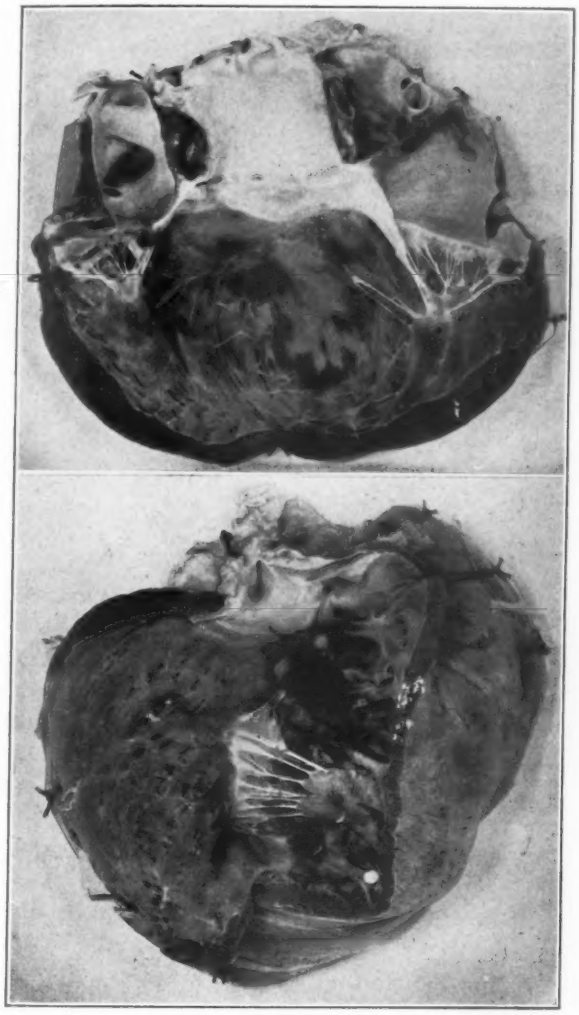


Fig. 6.—Experiment 51. Photographs of the endocardial surface of the left and right ventricles.

In a fourth experiment (Experiment 48) a septal infarct was produced accidentally. A large division of the septal artery lies just beneath the endocardium on the right side of the septum. In attempting unsuccessfully to cut the right branch of the His bundle this artery was severed. Electrocardiograms taken one week later were not strik-

ingly abnormal. They showed moderate left axis deviation with a prominent R spike in Leads I and II and large S deflections in Leads II and III. The infarct was not discovered until the heart was opened. It was visible only on the left side of the septum and was circular and about 3 cm. in diameter. The posterior subdivision of the left bundle branch crossed the region involved; the anterior subdivision did not.

COMMENTS

The experiments described are of interest from several points of view. The first (Experiment J) shows that the ligation of a coronary artery is followed by displacement of the RS-T segment of the ventricular complex even when the affected muscle lies in the septum and the epicardial surface of the heart is not involved. The last two experiments indicate that precordial leads may be of great value in locating the conduction defect when the ventricular complexes of the standard leads are of unusual outline. In bundle-branch block the precordial curves are often characteristic in every respect when the standard curves are not. The third experiment shows also that when the potential variations of the precordium are unusually small, the method of taking precordial leads in which a central terminal connected to the apices of the triangle formed by the three standard leads is used as the indifferent point has great advantages over that in which the indifferent electrode is placed on one of the extremities.

In the bovine heart, strands of Purkinje tissue which pass through the septum and join the Purkinje network of the right to that of the left ventricle have been described by Wahlin[4] and by Cardwell and Abramson.[5] Rothberger[6] has advanced the view that similar tracts of special tissue cross the septum in the dog's heart. If we understand him correctly, he believes that the destruction of these tracts should considerably increase the QRS interval of branch-block curves. Referring to Mahaim's views[7] with respect to the lesions responsible for the electrocardiographic changes attributed to arborization block, he suggests that widespread lesions of the septum which destroy the connections between the Purkinje systems of the two ventricles and also involve the bundle branches to a greater or less extent should produce curves of this kind. So far as our experiments have any bearing upon these opinions, they do not tend to confirm them. The QRS interval is apparently no greater in right branch block when it is produced by septal ligation than when it is produced by cutting the right branch of the His bundle. The ventricular complexes do not resemble those attributed to arborization block more in the one case than in the other. If connections between the terminals of the two bundle branches were present in our animals, it is of course possible that they escaped destruction either be-

cause they lay outside the infarcted region or because Purkinje tissue is less easily killed by cutting off its blood supply than is ordinary heart muscle. It is evident that some of the subdivisions of the left bundle branch which crossed the infarcted area continued to conduct. Lack of suitable equipment made it impossible to make serial sections of the infarcted region.

ORIGIN OF THE PRELIMINARY DEFLECTIONS OF THE LEVOCARDIOGRAM

The experiments under consideration and some observations made in experiments of the same series in which other coronary vessels were ligated are of interest from still another standpoint. In right branch block the deflections inscribed during the first part of the QRS interval represent the spread of the excitatory process over the muscle of the left ventricle. Each part of this muscle as it becomes active plays its individual part in the formation of these deflections. When a section of the septal or of the free wall of the left ventricle is dead, the electrical forces that it normally produces can no longer occur. A study of the ventricular complexes of dogs with right branch block and extensive infarcts of the left ventricular wall should therefore give some indication of the origin of the various deflections of the normal canine levocardiogram. In the case of septal infarcts all the subdivisions of the left branch of the His bundle cross the infarcted region. It cannot be assumed that these tracts always escape injury and that all the changes in the levocardiogram produced by ligation of the septal artery are due solely to destruction of the part of the left ventricular wall affected. Injury to the specialized tissues probably plays no important rôle in determining the alterations in the levocardiogram produced by infarcts of the free wall.

It should be pointed out also that the electrocardiographic changes that occur during the earlier stages of infarction are not due to death of the affected muscle. The immediate effects of coronary ligation are the result of injury to the cell membranes of the muscle fibers whose blood supply has been cut off; ten or twelve hours must elapse before the fatally injured tissues become incapable of producing potential differences. It may take even longer for the injury currents set up at the margins of the infarct to subside completely. We shall therefore consider only those electrocardiograms that were taken at least twenty-four hours after a coronary artery was ligated. The form of the canine levocardiogram varies considerably from animal to animal. Minor changes in this curve cannot be detected unless control curves from the same animal are available for comparison. Since such material is not at our disposal, we must be satisfied for the present with such information as may be obtained by comparing the right branch-block curves of dogs with extensive infarcts and those of healthy animals.

Some years ago Lewis[8] made a careful study of the ventricular complexes that characterize right branch block in the dog under conditions similar to those that obtained in our experiments. He found that the great majority of animals give concordant curves in which the chief initial deflection (S) is downward in all three leads. In his experiments its value in Lead I usually lay between 0.2 and 1.3 millivolts; in Lead III, between 1.1 and 2.5 millivolts. The preliminary deflections ordinarily consisted in a small downward movement (Q) followed by an upward excursion (R). The value of the former varied between 0 and 0.2 millivolt in Lead I and between 0 and 0.15 millivolt in Lead III; that of the latter between 0.1 and 0.3 millivolt in Lead I and between 0.2 and 0.9 millivolt in Lead III. In a few animals the levocardiogram was discordant, and the chief initial deflection of Lead I was upward. Lewis gave measurements of the curves obtained in twelve experiments; in half of these right branch block was produced by means of a clamp, and the possibility that some of the anterior subdivisions of the left bundle branch were damaged cannot be excluded. Similar measurements of the right branch block curves of twenty-two animals are shown in Table I (H2 to H18 inclusive). To conserve space, measurements of Lead II are omitted. Most of these curves were taken by Wilson and Herrman[9] in the course of their work on incomplete bundle-branch block. In all the experiments the animal was placed on its back and the chest was opened by splitting the sternum. In the last ten (H6 to H18 inclusive) one or more attempts to cut the left branch of the bundle were made before the right branch was attacked. In four (H7, H16, H17 and H22) of these ten experiments the cuts on the left side produced transient left branch block, but the ventricular complex regained its normal form before the right branch block was produced. No experiment is included in which the major subdivisions of the left branch were not intact when the heart was opened. With a few minor exceptions all the measurements fall within the limits given by Lewis. Table I also gives measurements of the right branch block curves of ten dogs with infarcts of various kinds (Experiments 46 et seq.). The curves are reproduced in Figs. 2 *B*, 4 *B*, and 7 *B*, *D*, *F*, *H*, *K*, *M*, *O* and *Q*.

The levocardiogram of the first animal (Experiment J) in which the septal artery was tied is of the discordant type, but all the deflections of Lead I are small. Since we cannot assume that the infarcted muscle was dead when the electrocardiograms were taken, this experiment is not suitable for our present purpose. The ventricular complexes of the second animal (Experiment 46) are of unusual outline, particularly in Leads II and III. In the latter lead, Q is abnormally deep and R is greatly exaggerated. The final downward movement (S) is less pro-

TABLE I

EXP. NO.	BICARDIOGRAM QRS INT. SECONDS	LEAD I Q	LEAD I R	LEAD I S	LEAD III Q	LEAD III R	LEAD III S	LEVOCARDIOGRAM QRS INT. SECONDS	LEAD I Q	LEAD I R	LEAD I S	LEAD III Q	LEAD III R	LEAD III S
H2	0.052	2.0	6.0	0.0	0.0	6.0	1.0	0.083	1.0	0.5	5.5	T	1.5	5.0
H3	0.048	0.0	5.0	0.0	T	18.0	1.0	0.075	0.0	1.5	4.0	0.5	7.0	8.0
H21	0.046	0.0	7.0	1.0	0.0	21.0	4.0	0.075	0.0	1.5	8.5	0.5	9.0	10.0
H26	0.052	0.0	3.5	0.0	1.0	20.0	9.0	0.074	0.0	3.0	5.0*	1.0	5.0	17.0
H28	0.052	0.0	6.0	0.5	0.0	14.0	8.0	0.091	0.0	5.5	4.0*	0.0	6.0	10.5
H29	0.050	0.0	8.0	T	0.5	12.0	1.0	0.078	0.0	4.0	6.0	0.0	9.0	8.5
H30	0.047	0.0	10.0	0.0	0.0	4.0	3.0	0.084	0.0	3.0	2.0*	0.0	1.0	10.5
H32	0.057	0.0	5.0	1.0	0.5	9.0	0.5	0.096	0.0	3.5	5.0*	0.5	3.5	12.0
M62	0.043	1.0	6.0	0.0	1.0	25.0	0.0	0.079	0.0	2.0	4.0	0.5	5.0	3.0
M60	0.042	1.0	8.0	0.0	1.0	17.0	1.0	0.068	1.0	1.5	10.0	T	11.5	12.0
H1	–	–	–	–	–	–	–	0.077	T	T	6.0	T	0.5	10.0
M56	–	–	–	–	–	–	–	0.076	0.5	1.0	6.0	0.0	13.0	16.0
H6	0.042	0.0	2.0	0.0	0.0	9.0	1.0	0.080	0.5	T	8.0	T	4.0	10.0
H7	0.053	1.0	7.5	0.0	0.0	5.0	4.5	0.086	0.5	1.0	0.5	0.0	1.5	10.5
H10	0.047	T	5.5	0.0	0.0	10.5	6.0	0.089	T	2.0	3.0	0.5	3.0	12.0
H12	0.041	1.0	5.0	0.0	0.5	15.0	0.0	0.083	1.0	0.5	9.5	0.5	5.0	8.0
H15	0.043	0.5	7.0	0.0	T	19.0	4.0	0.084	1.5	3.0	8.0	T	11.0	25.0
H16	0.044	1.0	5.5	0.0	0.0	13.0	7.0	0.072	1.0	1.5	6.0	0.0	5.5	16.0
H17	0.042	T	6.0	0.0	0.0	14.0	4.0	0.076	0.5	1.5	3.0	0.0	3.5	15.0
H22	0.046	1.0	5.0	0.0	0.0	16.5	3.5	0.070	0.0	0.5	7.0	0.0	1.0	15.0
H24	0.051	1.0	4.0	0.0	0.5	23.0	1.0	0.074	0.5	1.0	8.0	T	13.0	14.5
H18	–	–	–	–	–	–	–	0.089	0.0	0.0	7.0	0.0	6.0	10.0
46	–	–	–	–	–	–	–	0.080	0.0	6.5	7.5	3.0	26.0	8.5
51	–	–	–	–	–	–	–	0.083	0.0	2.5	3.0*	0.0	5.5	14.0
11	0.053	2.5	4.0	T	T	6.5	0.0	0.073	0.0	1.5	8.0	0.5	1.0	8.5
15	0.049	3.0	3.0	1.0	0.0	6.5	0.0	0.080	T	0.0	10.5	0.0	3.5	7.0
19	0.057	6.0	3.0	1.0	0.0	6.0	T	0.087	0.0	0.0	10.5	0.0	5.0	7.5
14	0.056	6.0	2.5	1.0	0.0	3.5	5.5	0.090	0.0	0.0	10.0	0.0	3.0	8.5
29	0.055	10.0	1.0	1.5	0.0	3.0	10.0	0.075	0.0	0.0	8.0	0.0	0.0	6.0
41	0.061	1.0	0.0	0.0	7.5	0.0	0.0	0.086	0.0	0.0	3.5	0.0	0.0	10.0
42	0.055	0.0	7.0	0.0	0.5	20.0	1.5	0.082	0.0	2.5	8.5	1.5	2.5	14.0
38	0.048	0.0	14.0	0.0	0.0	6.5	2.0	0.085	0.0	T	10.0	0.0	2.0	7.5

*In these instances S was followed by a conspicuous summit.

Measurements given in tenths of a millivolt. "T" equals trace.

nounced than usual. The onset of complete atrioventricular block with idioventricular complexes of varying form suggests that the left bundle branch was seriously damaged and eventually failed completely. It is possible that only a single subdivision was functioning when the first curves were taken. Ventricular complexes strikingly similar in form were obtained by Rothberger and Winterberg[10] (their Plate X, Figs. 8e and 8f) in an experiment in which they had cut the right and all the more posterior subdivisions of the left bundle branch. Complexes in which the chief initial deflection is upward in Lead III appear to be frequent under these circumstances. Such curves (Fig. 8 *H*) were obtained in one of our experiments in which the incisions on the right side of the septum were so deep that they reached almost through it. When the heart was opened an extensive extravasation of blood was found about the posterior branches of the left division. It seems probable that the peculiarities of the ventricular complexes in our second septal experiment were due mainly to blocking of these tracts. It is of course uncertain what effect opening the chest might have had upon the form of these curves.

In the third experiment (Experiment 51) the form of the branch block complexes is less unusual. They are not clearly outside normal limits. In view of the large amount of muscle infarcted this is somewhat of a surprise. It is probable, however, that if control curves from the same animal were available for comparison, definite changes could be detected.

The electrocardiograms taken before and after cutting the right branch of the His bundle in five experiments in which the anterior descending branch of the left coronary artery had been ligated at least twenty-four hours before are reproduced in Fig. 7. The bicardiograms are similar to the human curves obtained in coronary thrombosis affecting the same vessel.[11] In Lead I the first ventricular deflection (Q) is downward and is of large amplitude; in Lead III the first deflection is upward. The right branch block complexes of the first set of curves (Experiment 11) are not abnormal. The ligation operation was performed seventy-eight days before the electrocardiographic studies were made. There was an extensive subendocardial sclerosis on the ventral wall of the left ventricle; this lesion penetrated the wall over an area a centimeter or less in diameter. When the right side of the heart was opened, no cut crossing the course of the right division could be seen, but it is evident that this bundle must have been damaged. The second set of curves (Fig. 7 *C* and *D*) is from an experiment in which the infarct penetrated a narrow strip of the left ventricular wall on the left margin of the heart. The lesion was more extensive on the endocardial surface and involved the anterior papillary muscle. In three experiments (14, 19, and 29) the infarct was very large and involved the greater part of

the ventral and left lateral wall of the left ventricle, and the adjacent portions of the ventral wall of the right ventricle. In the branch block complexes of the last four experiments (15, 19, 14, and 29) the preliminary deflections (Q and R) of Lead I either are absent or are represented merely by an irregularity on the descending limb of the chief deflection (S), which is unusually deep. In the last experiment the preliminary deflections are absent in Lead III as well (Fig. 7-*K*). In this instance the apex and the apical third of the dorsal wall of the left

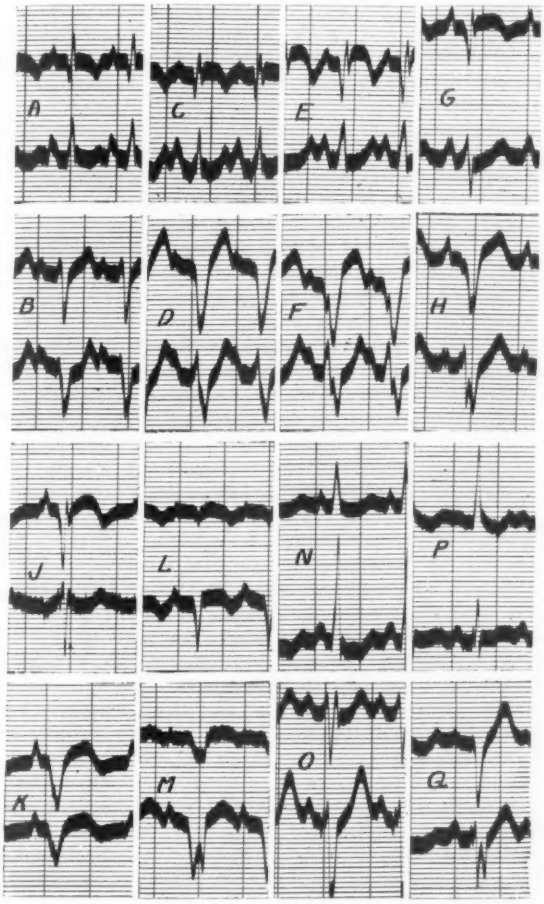


Fig. 7.—The bicardiograms (Leads I and III) and right branch-block complexes (same leads) of a series of dogs with myocardial infarcts. *A* and *B* are from Experiment 11, and were taken seventy-eight days after ligation of the anterior descending branch of the left coronary artery. *C* and *D* are from Experiment 15, and were taken twenty-four hours after ligation of the anterior descending artery. *E* and *F* are from Experiment 19 and were taken forty-eight hours after ligation of the anterior descending artery. *G* and *H* are from Experiment 14 and were taken forty-eight hours after ligation of the anterior descending artery. *J* and *K* are from Experiment 29 and were taken ninety-six hours after ligation of the anterior descending artery. *L* and *M* are from Experiment 41 and were taken forty-eight hours after ligation of the circumflex branch of the left coronary artery. *N* and *O* are from Experiment 42 and were taken forty-eight hours after ligation of the right coronary artery. *P* and *Q* are from Experiment 38 and were taken five days after ligation of the right coronary artery.

ventricle, as well as practically the whole of the ventral wall, were included in the infarct.

While it is true that either or both of the preliminary deflections of Lead I may be inconspicuous in the right branch block complexes of normal animals (see Table I), this is distinctly unusual, and the probability that it would occur accidentally in four experiments in succession is very small. We attribute the peculiarities of both the levocardiogram and the bicardiogram in these experiments to the absence of the electrical effects normally produced by the spread of the excitatory process over the infarcted region.

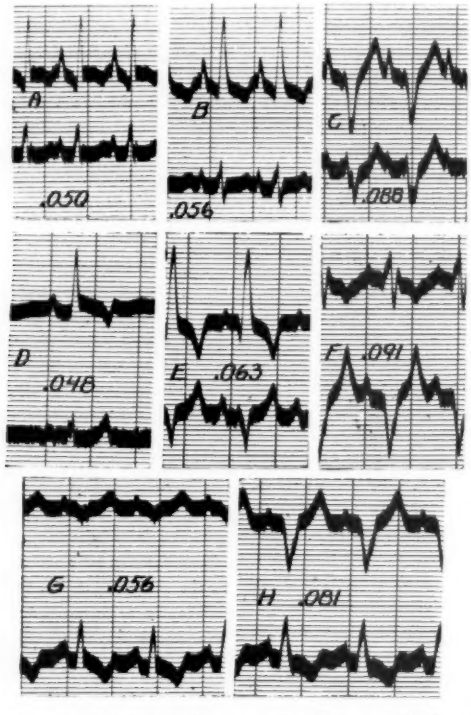


Fig. 8.—All records show Lead I and Lead III taken simultaneously. Figures written on the records give the QRS interval in seconds. Top row: Experiment 45. *A*, after opening the chest; *B*, after cutting the anterior subdivisions of the left bundle branch; *C*, after cuting the right bundle branch. Middle row: Experiment 50. *D*, after opening the chest; *E*, after cutting the anterior subdivisions of the left bundle branch; *F*, after cutting the right bundle branch. Bottom row: Experiment 13. *G*, after opening the chest. *H*, after cutting right bundle branch. There was pronounced extravasation of blood about the posterior subdivisions of the left bundle branch.

It should be pointed out that these changes are not due to damage to the anterior subdivisions of the left bundle branch, which transmit the excitation wave to the region affected. The electrocardiograms taken in two experiments in which these tracts were cut are reproduced in Fig. 8. It will be observed that the changes in the bicardiogram produced by this procedure are quite different from those observed follow-

ing ligation of the anterior descending coronary artery. The latter cannot therefore logically be attributed to intraventricular block affecting the tracts in question. Except for the absence of distinct preliminary deflections in Lead III in one set of curves (Fig. 8-*F*) the branch block complexes of these experiments are not unusual. The levocardiograms are not of the discordant type in which the chief deflection of Lead I is upward, as is often the case when the anterior branches of the left division have been injured.[10, 9] Ligation operations, partly unsuccessful,* had been performed on both of the animals used in these experiments. In each case a small infarct involving only the inner layers of muscle, and approximately a centimeter in diameter, was discovered when the left ventricle was opened. In one instance the lesion involved the base of the anterior papillary muscle; in the other it lay just above the apex of this structure. It seems unlikely that these infarcts had any important influence on the form of the ventricular complexes.

The sixth set of curves (L and M) shown in Fig. 7 is from an experiment in which the circumflex branch of the left coronary artery was ligated forty-eight hours before the electrocardiograms were taken. In Lead I the ventricular deflections of the bicardiogram are very small; in Lead III the first and chief deflection (Q) is downward. Similar changes in the bicardiogram in Lead III are seen in coronary thrombosis in man, when the infarct is on the posterior wall of the heart.[11] In the branch block curves preliminary deflections are absent both in Lead I and in Lead III. The last two sets of curves are from animals with infarcts of the right ventricle produced by ligation of the right coronary artery. In the bicardiograms the first ventricular deflection is upward in both Lead I and Lead III. In one instance the preliminary deflections of the levocardiogram are inconspicuous in Lead I, but the branch block curves are not strikingly peculiar in other respects.

While the experiments described do not enable us to identify with certainty the portions of the left ventricular muscle chiefly responsible for the various deflections of the canine levocardiogram, they offer a few valuable suggestions. Since the larger of the preliminary deflections (R) is preserved when a large part of the septum proper is destroyed, but tends to disappear when the free wall is extensively involved, it is hardly possible that this deflection can be of septal origin. The changes in the bicardiogram produced by infarcts that involve the ventral and those that involve the dorsal wall, respectively, would lead us to expect that this peak would be abolished in Lead I by infarcts of the former, and in Lead III by infarcts of the latter kind. This is essentially what we find to be the case. The infarcts produced by ligation of the anterior descending artery usually involve the left margin of the heart, and it is

*The large vessel selected for ligation was missed.

probably the activation of this portion of the wall that contributes most to R of the levocardiogram in Lead I. These infarcts also tend to involve the muscle to which the anterior margin of the septum is attached, but do not in the dog extend to the septum proper. The infarcts produced by occlusion of the posterior descending artery* usually face toward the left leg in man and toward the left hind leg in the dog. These parts of the wall when uninfarcted produce electrical effects that tend to make this extremity relatively positive, and are chiefly responsible for R of the levocardiogram in Lead III. Infarction of these parts, by subtraction of these electrical effects causes disappearance of the R deflection, and its replacement by a downward deflection in that lead. These infarcts also tend to involve the muscle to which the posterior margin of the septum is attached. We believe that the infarction of those portions of the wall attached to the septal margins is unimportant so far as the disappearance of the preliminary deflections of the levocardiogram is concerned† both in the case of ventral and in the case of dorsal infarcts. This muscle must be activated in the same general direction as the septum proper and should produce similar electrical effects.

The other preliminary deflection (Q) is inconstant in healthy animals, and its identification depends upon the presence of an R summit. Consequently, our observations throw very little light upon its origin. We may point out that a large Q deflection may be present in Lead III when a large part of the septum is dead (Fig. 2). It seems probable nevertheless that in normal animals Q of the levocardiogram is produced by muscle on the septal rather than by muscle on the left lateral side of the left ventricle. One should not be confused by a terminology that is convenient for the purposes of description, but has nothing to do with origins. The current terminology, which we do not propose to change, refers to Q as any initial downward deflection preceding the upstroke R; it is not concerned with the origin of this deflection. The small deflection under consideration is not analogous to the Q deflection of the human levocardiogram except in cases where the human levocardium is similar to that of the dog. When in branch block curves the chief and broadest QRS deflection in one lead is upward, the small depression that precedes it, though technically called Q, is really in causation analogous to a preliminary R deflection upside down.

In a previous article the view was advanced that the chief initial deflection of the levocardiogram (S) is not due to activation of the free

*In the dog this vessel is derived from the circumflex branch of the left coronary; in man it is usually derived from the right coronary.

†The form of the bicardiogram after ligation of the anterior descending or of the circumflex branch of the left coronary suggests that this procedure alters the form of the dextrocardiogram as well as that of the levocardiogram. After ligation of the former vessel stimulation of the anterior surface of the right ventricle may yield in Lead I complexes that begin with a deep downward excursion.

wall of the left ventricle, but is of septal origin. This statement referred, of course, to the descending limb of the large downward deflection in right branch block, and not to the later portions of this deflection which are clearly contributed by right ventricular muscle. One might therefore expect infarcts of the lateral wall to increase, and infarcts of the septum to decrease the size of this deflection. The matter is, however, somewhat complicated. First of all, we do not usually know in an individual case of right branch block at exactly what point right ventricular effects begin to modify the true levocardiogram. In the second place, infarcts of the lateral wall cannot modify deflections normally written by the septum after the activation of the lateral walls has been completed; septal infarcts cannot modify deflections ordinarily written by the right ventricle after activation of the septum has been completed. If the right ventricular effects are alone responsible for the deepest part of S, infarction of the septum can do no more than alter the position and slope of the descending limb of this deflection. Theoretically, infarcts of the septum and infarcts of the lateral wall of the right ventricle should, however, if the view under consideration is correct, algebraically diminish the area of the initial deflections in right branch block. Infarcts of the lateral wall of the left ventricle, on the other hand, should increase this area. The observations reported here do not either confirm or discredit the hypothesis that the chief deflection of the levocardiogram is of septal origin. The changes in S, if present, are not pronounced enough to enable us to detect them without control observations on the same animals made before the infarcts were produced. In the absence of control curves it has seemed useless to measure the areas of the initial deflections, a laborious operation. It may be noted that in the experiments in which the anterior descending artery was ligated S does appear to be unusually deep and the area of the initial deflections unusually small (absolutely large but negative in sign) in Lead I. In one of the septal experiments S is small and the area positive in the same lead. In Lead III, however, S is deeper and the area more negative in the latter experiment than in any of the former group. Since any conclusions must involve assumptions difficult to justify, it is not worth while to discuss this matter further at this time.

Since infarcts of the free wall modify R of the levocardiogram, at least part of the muscle affected must normally begin to produce potential differences very early in the QRS interval. We strongly suspect that practically all the endocardial surface of the left ventricle is already active when the upstroke of this deflection begins. Apparently the muscle that contributes to even the earliest ventricular deflections in standard leads is very widely distributed. For this reason it is difficult

to determine the origin of any of the QRS deflections in terms of the muscle region or regions responsible for them. Attempts to do so have often led to misconceptions.

One difficulty in the solution of this problem lies in the fact that the QRS group has no natural divisions. The first deflection, for example, varies from lead to lead in size, in direction and in duration. The muscle responsible for this deflection not only varies with the lead, but in any given lead is not necessarily the same in animals of different species nor even in different individuals of the same species.

SUMMARY

Ligation of the septal branch of the left coronary artery in the dog is usually followed by infarction of a large part of the ventricular septum. Immediately after this vessel is obstructed the electrocardiogram shows displacement of the RS-T segment of the ventricular complex. Later, disturbances of intraventricular or atrioventricular conduction develop; right bundle-branch block occurred in all three of our experiments. In one instance the right branch block complexes were not strikingly different from those usually obtained after the right branch of the His bundle has been cut, in spite of the fact that a large part of the septal muscle was dead.

In right bundle-branch block the precordial electrocardiograms may be characteristic in every respect when the standard electrocardiograms are not. Under these circumstances precordial leads are of great value in locating the conduction defect. When the potential variations of the precordium are small, the precordial electrodes should not be paired with a single electrode, but with a central terminal connected through like resistances of 5000 ohms or more to all three extremity electrodes.

The R deflection of the levocardiogram is not abolished by infarction of the septum but is frequently absent in Lead I after ligation of the anterior descending and in Lead III after the ligation of the circumflex branch of the left coronary. This deflection is not of septal origin. The muscle responsible for the preliminary deflections of the levocardiogram is widely distributed, and it is probable that most of the endocardial surface of the left ventricle is active before the first summit of the levocardiogram is written.

NOTE: We wish to thank Prof. C. V. Weller and the members of his staff for making and examining microscopic sections of the infarcts produced in our experiments.

REFERENCES

1. Lauterbach: Ztschr. f. d. ges. exper. Med. **41**: 665, 1928.
2. Wilson, Johnston, Macleod, and Barker: AM. HEART J. **9**: 447, 1934.
3. Wilson, Johnston, Hill, Macleod, and Barker: AM. HEART J. **9**: 459, 1934.
4. Wahlin: Upsala läkaref. förh. N. F. **34**: 769, 1928.
5. Cardwell and Abramson: Am. J. Anat. **49**: 167, 1931.

6. Rothberger: Ztschr. f. d. ges. exper. Med. **87**: 763, 1933.
7. Mahaim: Ann. de Med. **32**: 347, 1932.
8. Lewis: Phil. Trans. Roy. Soc. (London) Series B. **207**: 221, 1916.
9. Wilson and Herrman: Heart **8**: 229, 1921.
10. Rothberger and Winterberg: Ztschr. f. d. ges. exper. Med. **5**: 264, 1917.
11. Wilson, Macleod, Barker, Johnston and Klostermeyer: Heart **16**: 155, 1933.

THE INITIAL COMPLEX OF THE ELECTROCARDIOGRAM AFTER INFARCTION OF THE HUMAN HEART*

MAX WINTERNITZ, M.D.
PRAGUE, CZECHOSLOVAKIA

FOLLOWING the studies of Herrick,[1] Smith,[2] and Pardee[3] the changes in the final complex (T-wave) and in the S-T interval in cases of coronary sclerosis and thrombosis have been a fertile subject for clinical and experimental research. In contrast, the changes in the initial complex have, up to the present, received little attention. And yet from the first it must seem unlikely that the destruction, often so extensive, of part of the great connected mass of heart muscle should not be reflected in the process of activation of the ventricular muscle and in the corresponding electrical curve. Wearn[4] and after him a number of other writers have called attention to the decrease in the size of the ventricular waves following coronary thrombosis. Wilson[5] was the first to point out the appearance of a deep Q-wave in Lead III following coronary closure, a finding which has since received considerable attention. Fenichel and Kugell[6] extended these observations and held that an unusually deep Q in Leads I and II was also significant. Oppenheimer and Rothschild[7] found that infarction in the region supplied by the anterior descending ramus resulted in the changes described by them as arborization block, and Mahaim[8] made clear the relation between myocardial infarct and bundle-branch block.

None of the changes mentioned are pathognomonic for cardiac infarction. We may find low voltage, decrease in the size of the waves of the electrocardiogram, in all cases which are associated with severe impairment of cardiac function. We see this with about the same frequency in cases of acute myocardial infarct, in cases of severe infections or intoxications, in cardiac asthma and at the time of death. Moreover low voltage may be quite lacking in cases of arterial hypertension, or it may appear with pericardial effusion. As a sign we can put low voltage in the class with diminished heart sounds.

We may find a deep Q-wave with coronary thrombosis or with uncomplicated sclerosis, with left axis deviation, with scoliosis and also as a variation of the normal electrocardiogram.[9, 10]

Of more serious significance is the appearance of deep Q-waves in several leads which we occasionally find in chronic coronary occlusion and old infarcts. Freundlich,[11] to be sure, heeded this sign only when abnormal changes in the final complex were also present.

*From the First Medical Clinic of the German University in Prague, service of Dr. Rudolf Schmidt.

The question often arises whether there is not special difficulty in interpreting clinically the electrocardiogram, in how far the changes in the initial complex after coronary thrombosis can be attributed to this insult, when, as is usually the case, the form of the electrocardiogram before the insult is unknown. Since the coronary thrombosis is seldom the first or only pathological change in the heart, preexisting anomalies of the electrocardiogram must always be considered. This is particularly true in cases of arborization and bundle-branch block.

In the following discussion I shall report a series of cases which form a distinct group in that definite electrocardiographic changes of the QRS group correspond with definite myomalacia of the heart

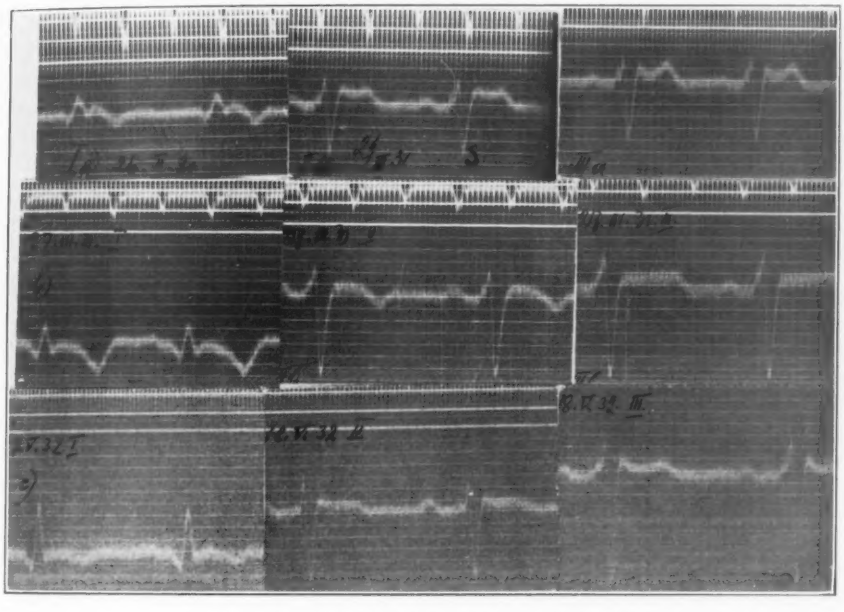


Fig. 1.—Case 1, attack on Feb. 24, 1931.

muscle and make it possible to diagnose myocardial infarct without knowledge of earlier electrocardiograms, of autopsy findings, or even at times of the clinical picture. In addition to our own cases we shall cite cases from the literature in which similar changes were present but not stressed by the authors. First I shall give abstracts of the clinical histories of our patients, mentioning only the essential points and showing only as many of the electrocardiograms as seem necessary.

CASE REPORTS

Case 1.—Forty-six-year-old letter carrier. Angina on effort since 1926. February 24, 1931, a typical attack with pain referred to the abdomen. Blood pressure on Feb. 26, 116/65 mm., on March 24, 95/65 mm. Recovery after eight weeks. In July, 1932, while taking CO_2 baths he had acute decompensation, and was admitted

to the clinic. Progressive cardiac failure and pulmonary infarction led to death on Aug. 22, 1932. Autopsy:* slight general arteriosclerosis with marked coronary sclerosis and extensive calcification, complete closure of the anterior descending ramus with area of myomalacia 12 cm. in diameter, aneurysm of the ventricular wall large enough to hold a man's fist associated with adherent pericardium, hypertrophy of the left ventricle and great hypertrophy and dilatation of the right ventricle, thrombosis of femoral vein, hemorrhagic pulmonary infarct, chronic passive congestion. Histological examination of the kidneys showed only congestion.

Electrocardiograms. The first electrocardiogram, three days after the insult (Fig. 1*a*), shows in Lead I the convex T-wave with high take-off from the descending limb of R, while in Leads II and III also T starts above the isoelectric level but lacks the characteristic coronary form, having a form which is not uncom-

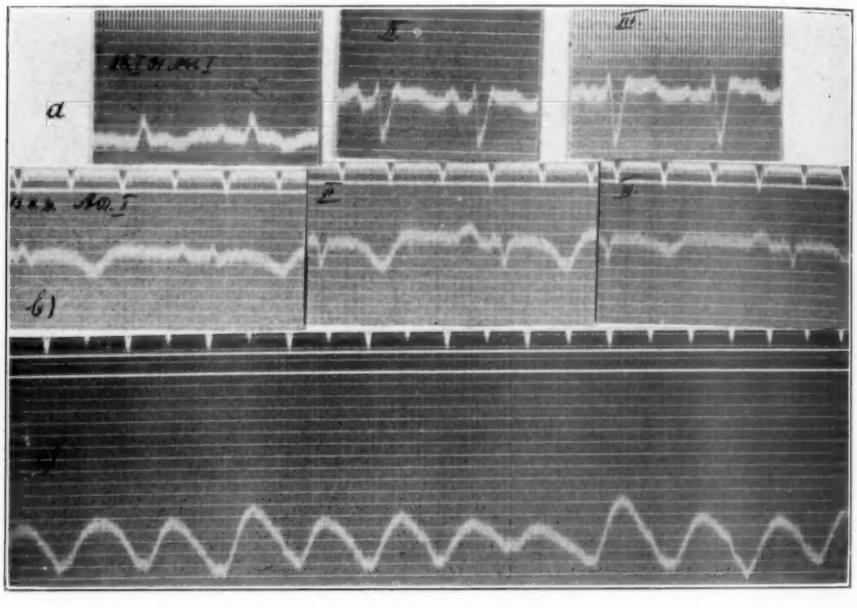


Fig. 2.—Case 2. (*a*) Twenty-four hours after the attack. (*b*) seventeen days after the attack, (*c*) after clinical death.

mon in these leads in cases of left axis deviation. Fig. 1 *b* and *c* also illustrates left axis deviation. One also notes the widening of QRS, just missing 0.1 sec. in Lead I and 0.11 sec. in Lead II. Lead I is not typical of left axis deviation in that there is only a rudimentary R following the broad Q-wave. The ratio of R_1, S_2 and S_3 is 3.5:15:14. After fifteen months we find Q_1 clearly formed and R_1 higher, just missing 9 mm. Left axis deviation, probably present before the insult, has reappeared.

Summary: Thrombosis of the anterior descending ramus with a large infarct and aneurysm in the area supplied by this vessel. In the acute and subacute stages the electrocardiogram showed, together

*All the autopsies reported were performed in the German Pathological Institute, Dr. A. Glon being chief.

with the typical T-wave changes, a left axis deviation but with very small R-waves. After fifteen months the R-waves had become upright.

CASE 2.—Turner, aged fifty-three years. Dyspnea on effort since 1920. January 27, 1931, pain typical of coronary closure, blood pressure at the onset 130/85 mm. On Feb. 17, after several days of tolerable condition, an attack of supraventricular paroxysmal tachycardia with rate of 220 and alarming collapse. As quinine, 0.2 gm. intravenously had no effect, 0.3 gm. was given three hours later. Death followed within a few minutes. Autopsy: advanced sclerosis of the left coronary artery, especially the anterior descending ramus with old thrombosis in its upper third and a resulting aneurysm involving the wall of the left ventricle, the septum and the apex; mural thrombus; thickness of wall of left ventricle in region of venous ostia 15 mm., in region of aneurysm 4 mm.; many smaller scars scattered through the muscle; slight sclerosis of the aorta; congestion and edema of the lungs; kidneys normal except for congestion.

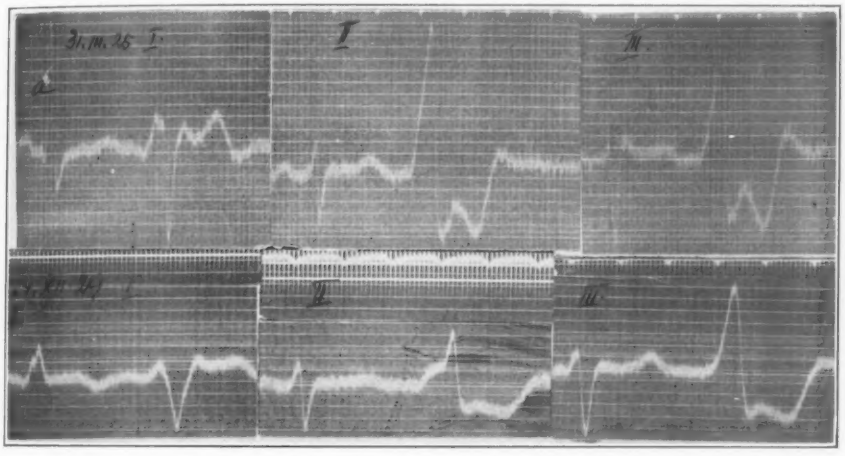


Fig. 3.—Case 3, attack in May, 1929.

Electrocardiograms. Fig. 2*a*, taken thirty-six hours after the insult, shows in Lead I a low R with typical high take-off and convexity of the R-T segment. Leads II and III show the prominent S of left axis deviation. In the next few days (Fig. 2*b*) the picture of low voltage appeared in all leads. T shows the characteristic changes. Fig. 2*c* shows the electrical activity of the dying ventricle.

Summary. Myomalacia with aneurysm of the wall in the area of distribution of the anterior descending ramus following acute coronary thrombosis. In the acute stages the electrocardiogram showed left axis deviation with noteworthy small R_1 and deep S_2 and S_3.

CASE 3.—Fifty-four-year-old woman with nephrosclerosis. Under the supervision of the clinic for years because of hypertension. Since the end of April, 1929, dyspnea and anginal pain on effort. In May, 1929, an attack of pain lasting fourteen hours, appearing without exciting cause, associated with extreme anxiety and dyspnea. After this, enforced bed rest for eight days. On June 11, 1929, blood pressure 185 mm., specific gravity of urine 1.006 to 1.018, angiospastic neuroretinitis, cardiac

decompensation. Since then constantly under observation in the clinic or as an ambulatory patient because of cardiac insufficiency. She was hypersensitive to strophanthin. Death on August 17, 1930, after several days of anuria from cardiac and renal insufficiency. Autopsy: generalized arteriosclerosis with marked sclerosis of the coronary arteries, particularly the anterior descending ramus, chronic aneurysm the size of a goose egg of the ventricular wall in the region supplied by this vessel; definite fibrous scarring of the heart and adherent pericardium; nephritis with marked shrinking of the glomeruli, and sclerosis of the afferent vessels.

Electrocardiograms. Fig. 3*a* shows the electrocardiogram four years before the insult, typical left axis deviation. A year later the picture was the same. Extrasystoles, always of the form shown, were observed for years. Fig. 3*b* shows the picture six weeks after the attack and was the form which persisted until death fifteen months after the attack. The R-wave of Lead I has become widened, splintered and of low voltage, while the Q-wave is even more prominent. A noteworthy change in the form of the ventricular extrasystoles has occurred. In a large collection of material we have seen only one other case—also a case of coronary thrombosis—in which there were such changes in the form of the premature beats.

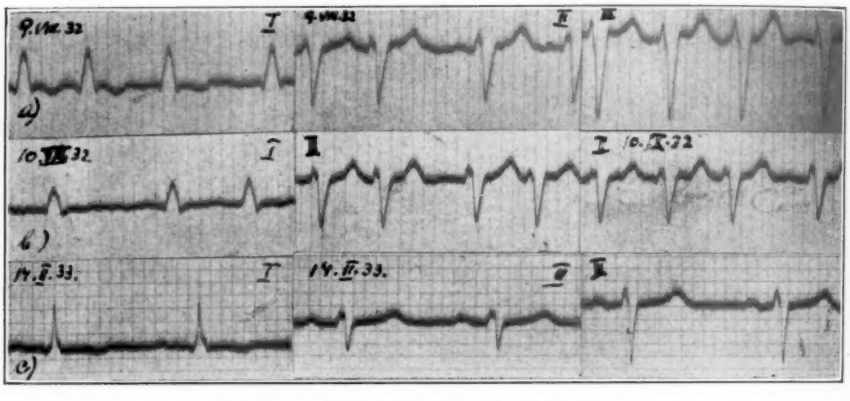


Fig. 4.—Case 4, attack August 4, 1932.

Summary. Clear-cut old myomalacia in the region supplied by the anterior descending ramus in a patient with hypertrophy of the left side of her heart and nephrosclerosis. The characteristic dwarfing of R_1 appeared six weeks after the attack and persisted until death, fifteen months after the attack. Unquestionable changes in the form of the extrasystoles, which presumably arose from the same focus, appeared after the attack.

Case 4.—Fifty-four-year-old housewife, in good health until August 4, 1932. On the afternoon of this day a sudden attack of vertigo forced the patient to lie down. A few hours later she had an extremely violent attack of pain associated with collapse and followed by dyspnea and fever. Admitted to the clinic August 6. Temperature 38.4°, blood pressure 120/80 mm., right hydrothorax, signs of pulmonary edema, heart somewhat dilated with feeble impulse a fingerbreadth outside midclavicular line, heart sounds feeble, systolic murmur at apex, pulse scarcely palpable, rapid and irregular. Recovery was interrupted by an attack of auricular

fibrillation on August 9 and 10. On August 12 auricular flutter which, because of the rapid ventricular rate (190 with two-to-one block), seemed to threaten life but which was overcome with quinidine, 0.8 gm. Further course uneventful. Blood pressure on August 29 was 95/70 mm. but later rose to 110/75. X-ray examination showed a dilated heart without characteristic form.

Electrocardiograms. Fig. 4*a* shows auricular fibrillation. In Lead I the form of T is so affected by the fibrillary waves that from it alone one could hardly make a diagnosis of coronary thrombosis. The initial complex shows a left axis deviation with R_1 smaller than S_2 or S_3. The decrease in size is even more apparent in Fig. 2*b*, taken six weeks after the insult. Six months after the attack (Fig. 4*c*) the R-waves had increased in size, and sinus rhythm had been reestablished.

Summary. A case of coronary thrombosis, without question from the clinical course, showed in its acute stages T-wave changes which were only suggestive, while the changes in the initial complex, low R_1 together with deep S_2 and S_3, were definite. Return of normal R_1 six months after the attack.

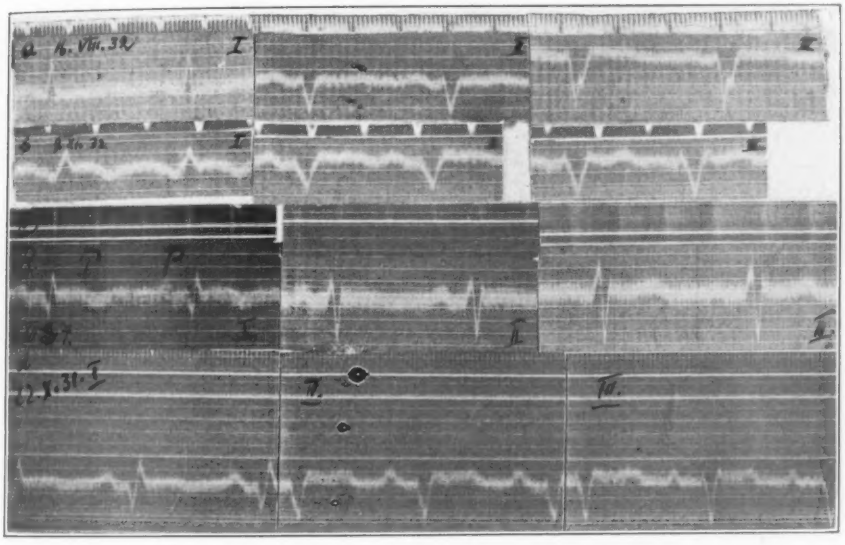


Fig. 5.—(*a*, *b*) Case 5, attack November 6, 1932.
(*c*) Case 8, attack November 13, 1927.
(*d*) Case 9, attack in May, 1931.

CASE 5.—Forty-nine-year-old office worker. In January, 1929, began to suffer from nocturnal anginal distress. Symptoms soon appeared on walking but were never paroxysmal in character. In August, 1929, he entered the hospital because of an exacerbation of the symptoms. Except for distant heart sounds there were no abnormal cardiac findings. Blood pressure 130/75 mm. Unexplained elevation of temperature. Good effects from luminal and hormocardiol. After discharge he returned at once to his work (which involved much stair climbing) and almost immediately was attacked by sternocardia and epigastric pain. On the night of November 6, 1932, he was wakened by a terrific attack of pain associated with

angor animi and sense of suffocation. The next day he was moved, in a state of collapse, still with severe pain, and with a temperature of 38.6°. After a short period of improvement the picture was complicated by extrasystolic ventricular tachycardia with a rate of about 150. He died November 17. Autopsy: high grade selerosis of coronary vessels, almost complete old closure of circumflex branch of left coronary, old malacia of the posterior wall of the left ventricle, closure of anterior descending branch in its upper third with recent necrosis of the anterior wall of the left ventricle from basal portion to the apex, scarring of the septum, eccentric hypertrophy of the right side, chronic passive congestion.

Electrocardiograms. Fig. 5*a* is one of many electrocardiograms taken between August 22, 1929, and August 16, 1932. All showed a picture, not at all striking, of left axis deviation with relatively low waves, flat T and slight slurring of S in Leads II and III. Fig. 5*b*, taken three days after the second attack, shows a small Q_1 followed by a reduced R, but only slight decrease in the size of S_2 and S_3. T_1 shows an upward convexity. In the following days, with the decreasing size of all waves, R_1 disappeared almost completely.

Summary. Two attacks of coronary thrombosis, the first involving the circumflex and leaving no clear-cut electrocardiographic evidence.

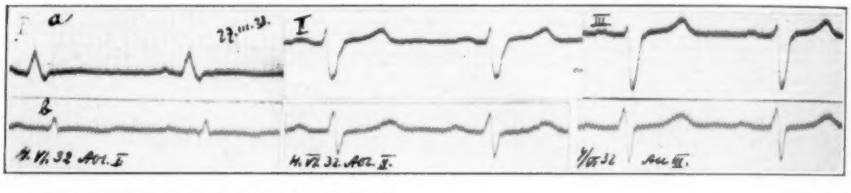


Fig. 6.—(*a*) Case 6, time in 1/20 sec.
(*b*) Case 7, four days after the attack.

Three years later occlusion of the anterior descending ramus led to malacia and in the electrocardiogram almost complete disappearance of R_1 while S_2 and S_3 remained relatively well formed.

CASE 6.—There is little information concerning this case, that of a sixty-seven-year-old man who visited the clinic only once as an ambulatory patient. For several months he had suffered from arthritis of the left shoulder and complaints interpreted as anginal. Electrocardiogram was taken because the fluoroscopic picture showed a striking deformity of the left side of the heart interpreted as an aneurysm of the ventricle. Blood pressure 160 mm. Hg.

Electrocardiogram. Fig. 6*a* shows a record made with Sieman's oscillograph. In all leads QRS is widened to approximately 0.12 sec., but lacks the great size and bizarre form characteristic of complete bundle-branch block. The small R_1 contrasts sharply with the deep S_2 and S_3.

Summary. Clinical and roentgenological findings to support the diagnosis of aneurysm of the wall of the left ventricle, broad left form of electrocardiogram with striking decrease in R_1 compared with deep S_2 and S_3.

CASE 7.—Fig. 6*b* was derived from a seventy-three-year-old patient and was taken outside. According to the report of the attending physician the patient had had a typical attack of coronary thrombosis four days earlier. Blood pressure was normal before the attack.

Electrocardiogram. Another record showing left axis deviation but in this case definite R-waves are present in Leads II and III. Contrast the tiny R_1 with the well-marked S_2 and S_3. T_1 inverted. P-R interval 0.20-0.21 sec.

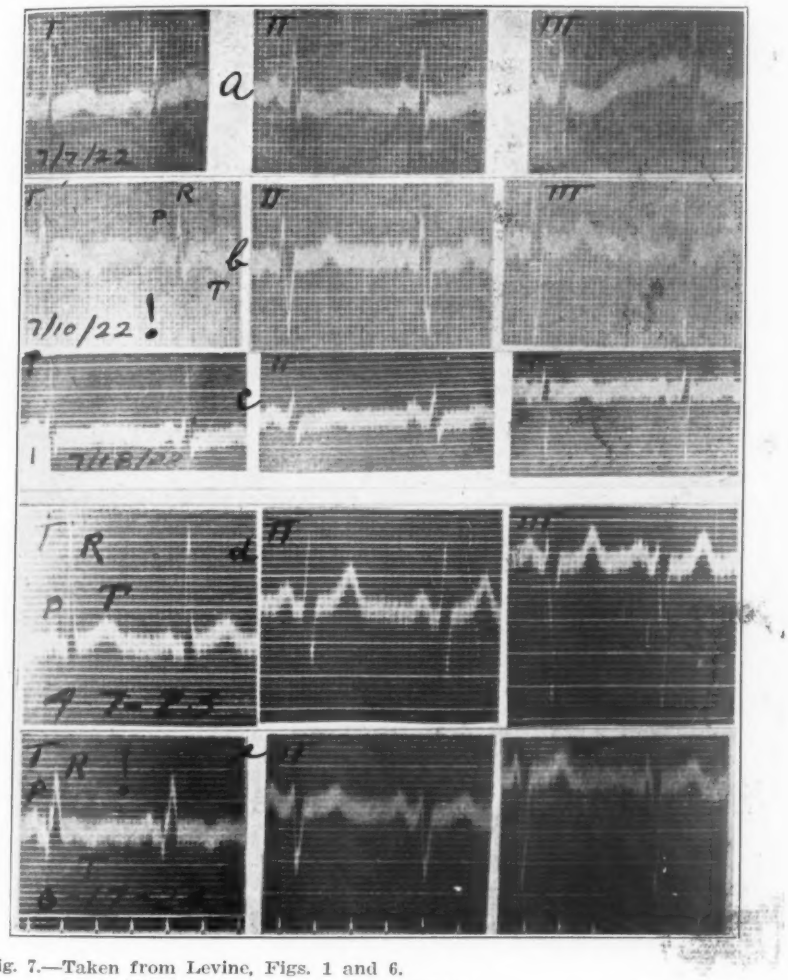


Fig. 7.—Taken from Levine, Figs. 1 and 6.
(*a-c*) Attack July 6, 1922, good recovery.
(*d, e*) Attack April 8, 1923, death three years later, no autopsy.

Summary. Four days after acute coronary closure the electrocardiogram suggests myocardial infarct because of the contrast between a diminutive R_1 and a clear-cut S_2 and S_3.

We shall consider with these cases several definite cases of coronary thrombosis taken from the literature and belonging in the same group.

Levine[12] in his monograph cites 82 incontestable cases of coronary thrombosis in which electrocardiograms were taken, in some cases both before and after the attack. Of these cases 12 belong in our group, those shown in Levine's Figs. 1, 4, 6, 8, 17, 30, 41, 43, 61, 70, 76 and 77. Figs. 7 to 10 are reproductions from Levine's classic material. In three cases one can follow the development of the changes from simple left axis deviation. Five cases were controlled by autopsy

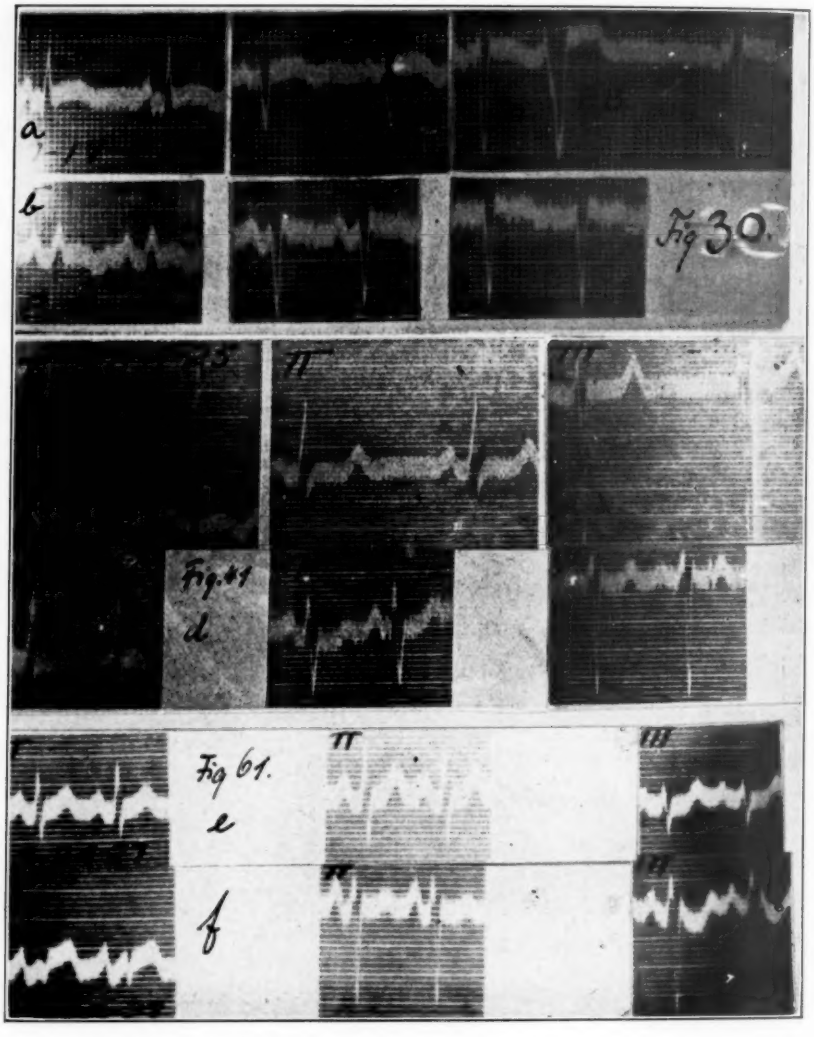


Fig. 8.—From Levine, Figs. 30, 41, 61.

(*a, b*) Attack July 4, 1922, death August 8, 1922, infarct of the left ventricle with rupture.

(*c, d*) Infarct August 25, 1925; death August 31, 1927. Mesaortitis, stenosis of ostia of coronary vessels, acute infarct of the left ventricle. According to Levine, "Electrocardiogram without definite changes." Note S-T in Lead II!

(*e, f*) Attack March 20, 1927, good recovery in spite of paroxysmal ventricular tachycardia.

and infarction of the left ventricle was found in all. In three cases the anterior descending ramus of the left coronary artery was the site of the thrombosis, and in two cases the location of the closure was not mentioned. In two cases there was definite aneurysm of the ventricle in the area supplied by the occluded vessel. Fig. 10*c* is taken from Dressler's[13] atlas and shows the same type of case. The author noted that the tracing was from a case of luetic aortic aneurysm and that it resembled the tracings seen in cases of coronary closure. As a matter of fact the appearance of T_1 strongly suggests the presence

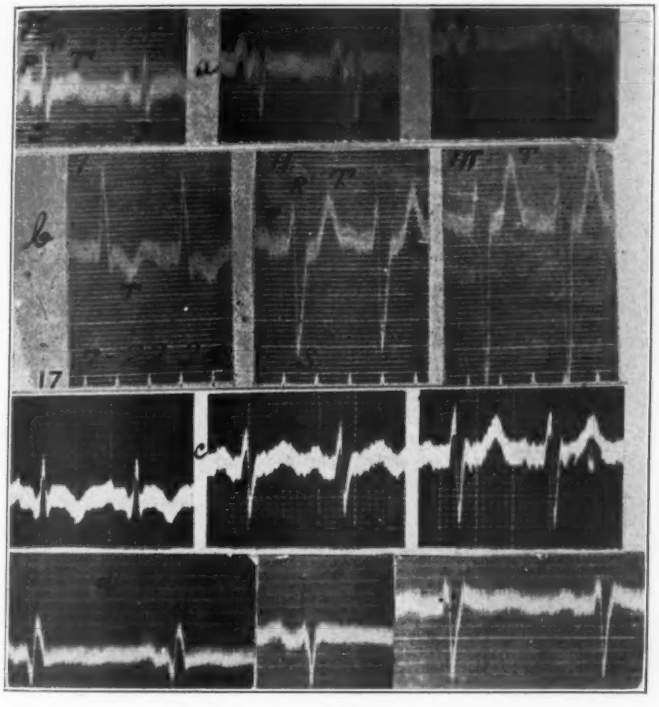


Fig. 9.—(*a-c*) From Levine, Figs. 4, 17, 43. (*a*) Attack May 2, 1927. Wassermann reaction +++, good recovery. (*b*) Attack July 20, 1924; autopsy, thrombosis of anterior descending ramus. (*c*) Attack November 26, 1926, recovery, later death without autopsy. (*d*) From Freundlich, Fig. 11. Three months after attack.

of luetic coronary occlusion with resulting myomalacia. In Fig. 73 of his book Mahaim[8] shows the tracing of a case which was confirmed by autopsy and which is here reproduced in Fig. 10*d*. Autopsy showed embolic (?) closure of the anterior descending ramus with typical localized infarct and aneurysm of the heart wall. We shall return to the histological picture later. Fig. 10*e*, taken from Condorelli's book,[14] is derived from a case of coronary thrombosis which showed at autopsy closure of the left coronary with infarct in its area of distribution. In one of Smith's[15] cases (his Fig. 3) the record taken a

few days after the attack shows a picture similar to that which we have illustrated in Figs. 1 to 5. Autopsy showed closure of the anterior descending ramus and of two smaller branches of the circumflex ramus with definite myomalacia at the apex of the left ventricle. In Oettinger's[16] work we find that the case illustrated in Figs. 3 to 6 belongs

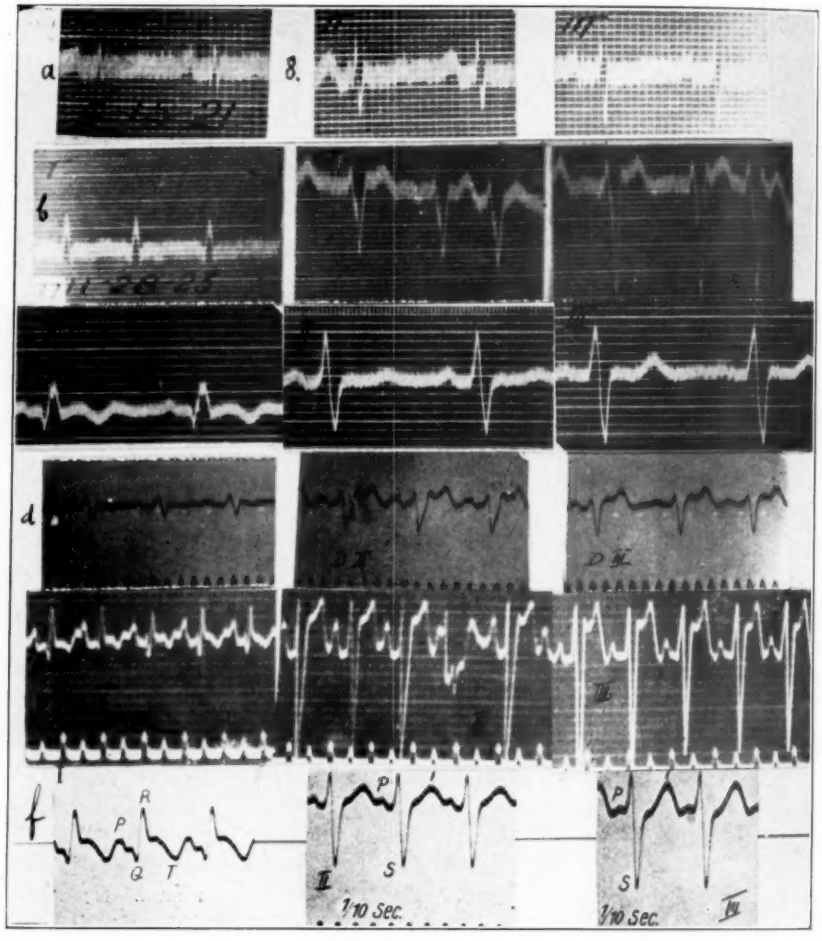


Fig. 10.—(*a*) Levine, Fig. 8. Attack June 10, 1921; death June 22; blood pressure had been 200.
(*b*) Levine, Fig. 77. Attack October 18, 1923, death December 3, 1923, almost complete closure of anterior descending ramus.
(*c*) From Dressler, Fig. 22 (see text).
(*d*) From Mahaim, Fig. 72 (see text).
(*e*) From Condorelli, Fig. 67. Seven months after the attack, seven days before death, thrombosis of the left coronary artery, large infarct of the apex and anterior wall of the left ventricle.
(*f*) Oettinger, Fig. 6. Thrombosis of the anterior descending ramus.

in our group (see Fig. 10*f*). This also showed occlusion of the anterior descending ramus post mortem. Also in the recent work of Freundlich[11] we can recognize in Figs. 11 and 12 (see Fig. 9*d*) similar changes

in the QRS group. This tracing came from a case of severe angina pectoris three months after coronary closure. We are convinced that further examination of the literature would reveal still more cases of this sort.

The second group, to which we shall now pass, is closely related to the first. The first two cases mark a direct transition.

CASE 8.—A forty-three-year-old official arrived on November 13, 1927, after a tiring motor trip to visit his wife in a sanatorium. On the way he had had a violent attack of stenocardia which had forced him to interrupt his trip and to rest for several hours in a hotel room. The physician who was called stated that the temperature was 36.5°, pulse 120 and small, cardiac dullness normal. The pain disappeared after medication. On November 15 x-ray examination showed the heart at the anterior axillary line, temperature 38.6°. Patient was admitted to the clinic on November 28. His father had died of a heart attack and one brother of heart disease. He smoked 20 cigarettes a day, used alcohol to excess, denied syphilis. Wassermann reaction was negative in the blood and spinal fluid. Heart dullness normal, scratchy systolic murmur at Erb's point. On x-ray examination the shape of the heart was not characteristic, greatest transverse diameter 13.5 cm. Blood pressure 105 mm. No pain.

Electrocardiogram. Fig. 5*c* shows in Lead I a deep Q-wave followed by an R of the same height; T-wave shows bowing above the isoelectric line and is inverted. Leads II and III show small R- but deep S-waves; T_2 and T_3 not striking. QRS is of normal duration.

Summary. Clinically this was certainly a case of coronary thrombosis. Four weeks after the attack the electrocardiogram showed suspicious changes in the final complex in Lead I, and an initial complex with the main deflection downward in all leads.

CASE 9.—A fifty-four-year-old mason was taken sick in May, 1931, with anginal distress. The individual attacks were of short duration, not very violent, repeated more than ten times in one day. After several days' rest in bed he returned to work but experienced anginal pain on effort. On August 22, 1931, he noted edema for the first time. In September he had cardiac asthma that did not recur after digitalis. From then on he had permanent decompensation and attacks of angina. Blood circulation time (decholin method) 38 sec. (normal up to 16 sec.). X-ray examination showed the heart to be dilated to both sides but without characteristic form. Faint heart sounds. Blood pressure 85 mm. Under constant observation, last seen in January, 1933.

Electrocardiogram. Fig. 5*d*. The picture is very similar to that of the preceding case. Again there is a deep Q in Lead I and the chief deflection is downward in Leads II and III. The R-T segment is so uncharacteristic that from it alone the diagnosis of coronary thrombosis could not be made. Three months later, about eight months after the onset, the electrocardiogram was practically unchanged.

Summary. Gradual development of myomalacia of the left ventricle. Following the attack and eight months later the initial complex of the electrocardiogram was directed downward in all leads. The final complex hardly suggested infarction.

CASE 10.—Fifty-four-year-old working woman. Brief attacks of pain in the region of the heart commenced in February, 1932, became more frequent; and on March 30 there was a very severe attack of pain and oppression. On April 10 a most intense attack associated with vomiting, fear of death, and cold sweat. Findings on April 13, patient in grave state of collapse without edema; left arm and side of chest felt warmer than the right, tenderness over areas supplied by the left trigeminal nerve and brachial plexus. Severe precordial pain which decreased after camphor given intravenously. On April 20 the patient, who had been progressing well, had an attack of auricular fibrillation which stopped spontaneously. After this, hemiplegia. Death on May 1. Autopsy: marked general arteriosclerosis, particularly of the cerebral, sacral and mesenteric vessels, thrombosis of the anterior descending ramus with resulting area of infarction measuring 8 × 5 cm., involving the septum and anterior wall of the left ventricle, mural thrombus attached to the ventricular aneurysm, localized adherent pericardium, embolism of right middle cerebral and renal arteries, infarct of spleen.

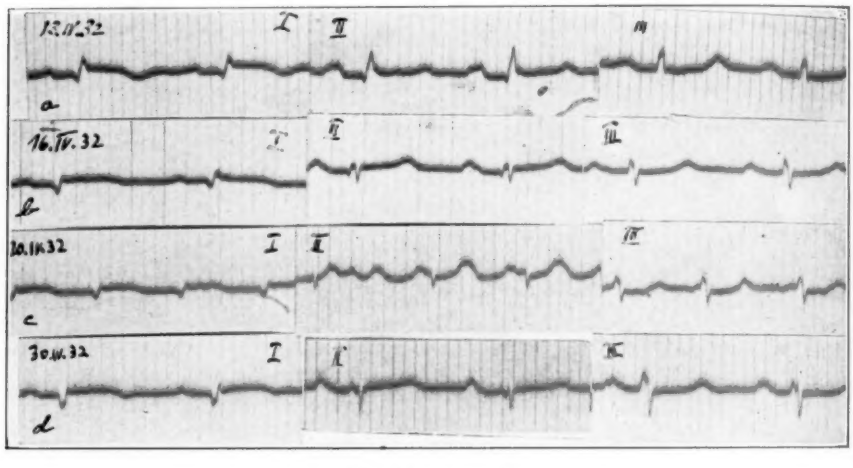


Fig. 11.—Case 10.

Electrocardiograms. In Fig. 11*a* narrow excursion of all waves, small Q in Leads I and II. T_1 shows high take-off, is prolonged and convex in form. In Fig. 11*b* waves still smaller, small S in Leads II and III. In Fig. 11*c* auricular fibrillation with coarse fibrillary waves. In Fig. 11*d* sinus rhythm restored; R_1 and R_2 absent; initial complex downward in all leads. T-wave permits recognition of the insult only on closest inspection.

Summary. Thrombosis of the anterior descending ramus with the formation of a large aneurysm of the ventricle. The initial complex, at first not characteristic, assumed a characteristic form after seventeen days so that finally it was directed downward in all leads.

CASE 11.—A sixty-year-old business man. Dyspnea on effort since 1923, in 1929 diabetes mellitus established; since the end of 1929 edema at the end of the day. In winter of 1930 massive edema; confined to bed since then. Admitted to the clinic March 30, 1932, with extreme decompensation, pulsus alternans, edema, con-

gestive effusions. On examination feeble impulse in anterior axillary line, heart sounds almost inaudible, blood pressure 150/115 mm. *Cor bovinum* on x-ray examination. A fair diuresis with novurit and ammonium chloride. Allowed to go home and died soon thereafter.

Electrocardiogram. Fig. 12*a*. The initial complex shows slight notching in the first two leads, no R in Leads II and III, S relatively well defined in all leads. T-waves are almost isoelectric, suggesting poor compensation. Duration of QRS is 0.09 sec. P-R interval is 0.1 to 0.12, and there is no isoelectric line between P and R.

Summary. A badly damaged heart, apparently as the result of hypertension. The electrocardiogram failed to show the expected left axis deviation, and the initial complex was directed downward in all leads.

Case 12.—A seventy-four-year-old guide on March 19, 1932, while walking was seized with an attack of severe breathlessness and cough which disappeared after he

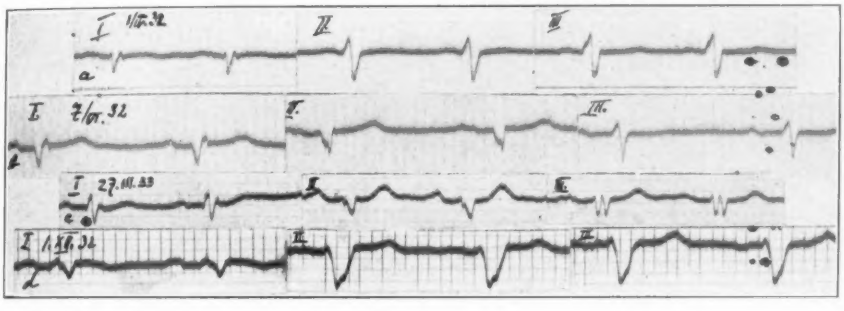


Fig. 12.—(*a*) Case 11.
(*b*) Case 12. Attack March 19, 1932; death January 10, 1933; large aneurysm of the anterior wall of the left ventricle.
(*c*) Case 13. Attack October 19, 1932.
(*d*) Case 14. Attack October 13, 1932.

had stood still for a few minutes. That night he had a severe attack of dyspnea with violent anginal pain "as if his heart was being crushed with red hot pliers." The attack lasted three hours. After this he had orthopnea at night and in the middle of May edema. On June 6, 1932, he was admitted to the clinic in a state of severe decompensation. He was found to have a heart dilated to left and to right, without characteristic form, distant dull sounds without accentuation, blood pressure of 180/105 mm. emphysema, Wassermann reaction negative. Death occurred on January 10, 1933, apparently from cardiac insufficiency. Autopsy: high grade coronary sclerosis with marked stenosis of the anterior descending and circumflex branches of the left coronary artery, old aneurysm measuring 10×5 cm. involving the septum and apex of the left ventricle, marked sclerosis of the aorta, chronic passive congestion.

Electrocardiogram. Fig. 12*b* shows one of several electrocardiograms taken at various times. R-wave completely absent in Leads I and II, rudimentary in Lead III. S-wave present in all leads, notched in the second. In Lead I, S is followed by a small positive deflection that might be called R, in which case S might be described

as a deep Q. In any case the principal deflection is downward in all leads. T_1 and T_2 are upright. T_3 is shallow and inverted but not characteristic. QRS is of normal duration.

Summary. Badly decompensated heart with area of myomalacia three to eight months after acute coronary closure, narrowing of anterior descending and circumflex branches with aneurysm. The initial complex of the electrocardiogram directed downward in all leads, but apart from this no electrocardiographic evidence pointing to infarction.

CASE 13.—Forty-eight-year-old factory manager, formerly well, heavy cigarette smoker. On the evening of October 19, 1932, after straining at stool, had terrific attack of precordial pain which lasted one hour and was associated with sweating and fear of death. One week later nocturnal return of pain leaving him very weak for two or three days. Since then angina on effort and exhaustion on the least exertion, but comfort when at complete rest. On March 27, 1933, no abnormal findings on physical examination, blood pressure 125/70 mm.

Electrocardiogram. Fig. 12*c*. At this time the patient was taking small doses of digitalis. The R-wave is apparent only as a small notched elevation in Lead I, absent in the other leads. S is low but definite in all leads, moderately splintered in Lead II, and grossly splintered in Lead III to form a *W*. QRS is of normal duration. The slight depression of S-T and T in Lead I is not remarkable and may be the result of digitalis.

Summary. From the clinical course a coronary thrombosis with secondary myomalacia is most probable. Electrocardiograms five months after the attack and later showed no characteristic changes in the final complexes. The initial complex shows, together with low voltage and notching without widening, a definite preponderance of the negative as compared with the positive waves.

CASE 14.—Sixty-three-year-old pensioner. For four years angina on effort and dyspnea while working. On the evening of October 13, 1932, after leaving the inn where he had consumed two liters of beer, he had violent cramplike pain in the epigastrium extending upward under the manubrium and lasting twelve hours. The next day he walked to the office of his physician, who found that the blood pressure which formerly measured 160 mm. had dropped to 95 mm. On the way home another attack of pain prevented him from continuing on foot. He got up after a week in bed, but felt very weak and was short of breath on slight exertion. On December 1, while returning from a visit to his physician, he had a severe attack of cardiac asthma in which he was brought to the clinic. Family history not remarkable. He did not smoke more than 12 cigarettes, denied syphilis. Examination showed a heart enlarged to the left, feeble sounds and definite gallop at the apex, blood pressure 115 mm., temperature normal, leucocytes 14,000, aortic configuration of heart on x-ray examination and on the left border a bulging which showed slight pulsation (aneurysm).

Electrocardiograms of November 17, December 1, 2, and 4, were practically identical and showed (Fig. 12*d*) sinus rhythm, normal P and P-Q, QRS duration of 0.13 sec. The principal deflection is downward in all leads, initial complex very

low and somewhat notched in Lead I; in Leads II and III a moderately deep S-wave with definite notching of the up-stroke. The S-T segment is somewhat above the isoelectric level in Leads I and II, but this is significant only in Lead I, since T is inverted in this lead. In Lead III there is some change in the S-T segment as S fails to reach the isoelectric line, a change often associated with bundle-branch block.

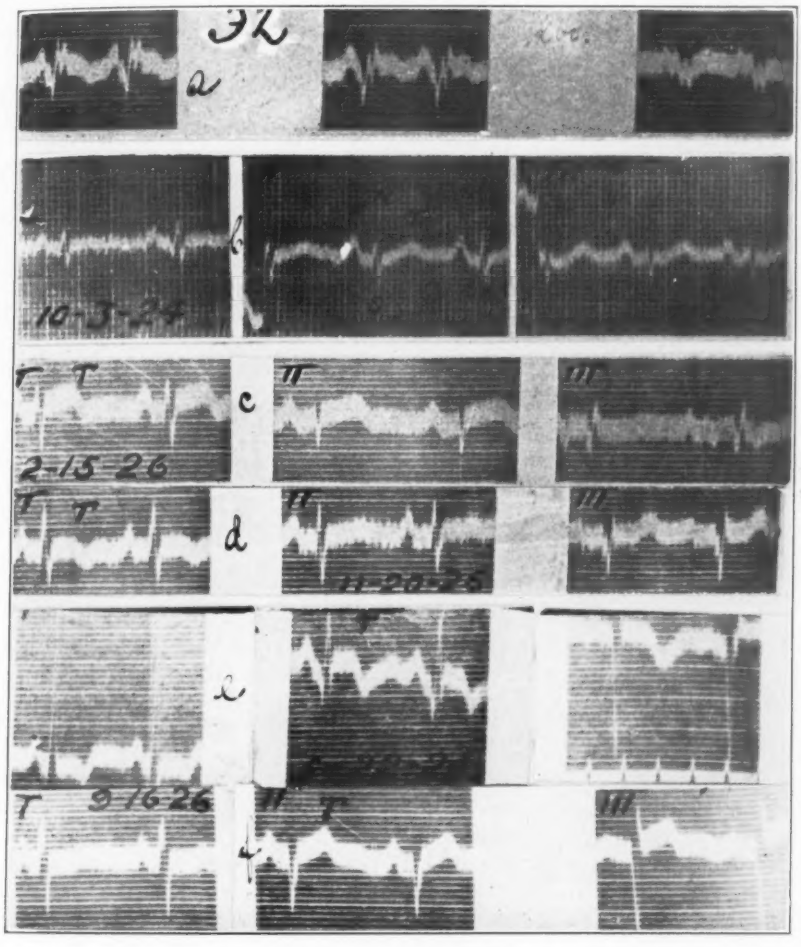


Fig. 13.—From Levine, Figs. 32, 36, 44*b*, 44*e*, 40*a*, 40*h*.
(*a*) Attack December, 1927; autopsy, thrombosis of anterior descending ramus. (*b*) Attack June 21, 1924, recovery. (*c*) (*d*) Attack February 4, 1926, recovery, persistence of Type b_{1-3} for a long time. (*e*) (*f*) Attack June 17, 1924; autopsy, thrombosis of anterior descending ramus, aneurysm of heart wall. Gradual appearance of Type b_{1-3}.

Summary. Clinically and roentgenologically there is little doubt that this was a case of coronary thrombosis with a large aneurysm of the left ventricle. Electrocardiograms, five to seven weeks after the attack, showed a severe disturbance of intraventricular conduction

and a preponderance of all the negative waves of the QRS group, but in the final complex only a suggestion of the changes associated with coronary thrombosis.

We can also add to this group several examples from the literature. Fig. 13 is a reproduction from Levine's monograph. In all four cases there was unquestionable coronary thrombosis which in the cases represented by Fig. 13 *a* and *c* was found at autopsy to involve the anterior descending ramus. Of particular interest is Case 13 c, d which, eleven days after the insult (c) still showed typical left axis deviation, while the characteristic changes did not appear until one month after the insult nor did they show complete development for two months more.

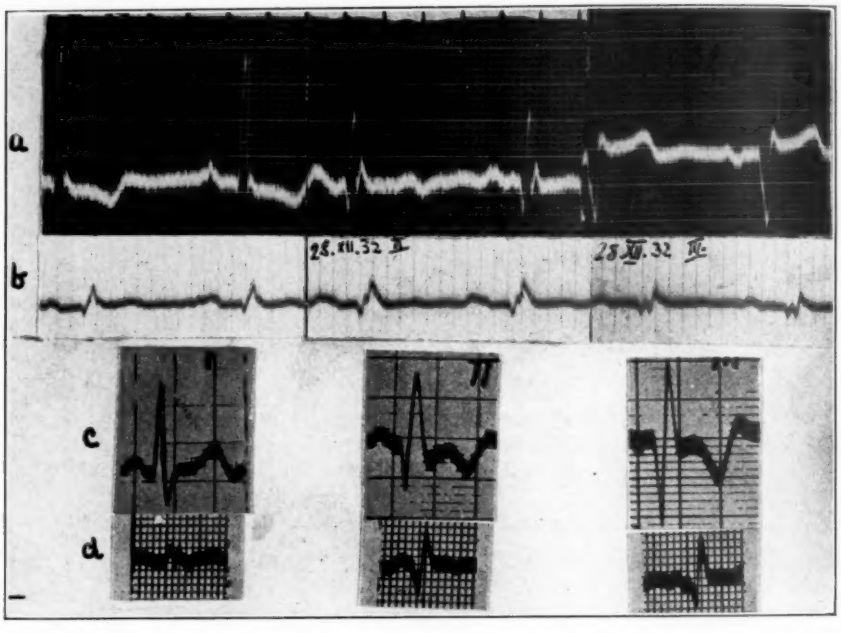


Fig. 14.—(*a*, *b*) Case 14. Before and after the second attack on December 24. (*a*) With Boulitte's string galvanometer, (*b*) with the Sieman's oscillographic machine.
(*c*, *d*) From Cooksey and Freund, Fig. 4*a* and *f*. Three weeks after the first attack and forty-eight hours after the second (see text).

Smith[15] in his paper shows a striking case in which one month after coronary closure the initial complex was directed downward in all three leads. (See Fig. 4*b* of Smith's article.)

In its final picture the last group is less sharply defined than either of the foregoing. It is noteworthy, however, for the fact that changes in the preexisting electrocardiogram appear suddenly, almost without transitional steps, following the coronary closure.

CASE 15.—A sixty-five-year-old retired official who had suffered from stenocardial oppression for a long time was admitted to the clinic on December 25, 1932,

in a state of collapse with severe dyspnea. For a time he complained of painful sense of pressure in his chest which interfered with breathing. He had no edema, some cyanosis, respirations thirty with a suggestion of periodic character. Other physical findings negative except for faint heart sounds, blood pressure 125/80 mm. Wassermann reaction negative. After strophanthin and hexeton intravenously he had relief from pain and dyspnea. Still his condition remained grave, and on December 31, twenty minutes after the injection of strophanthin, 50 mg., he became intensely cyanotic, stopped breathing and died. Autopsy: marked sclerosis of the arteries at the base of the brain and of the coronary and abdominal vessels; thrombosis in its middle third of the circumflex branch of the left coronary; almost complete closure in the upper and complete closure in the middle third of the anterior descending branch; scar, measuring 4×5 cm., on the posterior wall of the left ventricle and recent softening of the lower third of the anterior wall, the apex, and the lower part of the septum extending to the lower part of the right ventricle; mural thrombus attached to the infarcted area; thrombi in the periprostatic plexus, thrombosis of the spleen, recent portal thrombosis; embolism to pulmonary artery supplying right upper lobe; chronic passive congestion; hypertrophy of right ventricle.

Electrocardiograms. Fig. 14*a* is a record taken two months before death, apparently after the first attack involving the circumflex ramus and before the second attack involving the anterior descending ramus. These records were taken with Boulitte's string galvanometer, and we are indebted to Dr. E. Weitels for his courtesy in allowing us to reproduce them. The tracing shows typical left axis deviation with large excursions. In Lead I there is a suggestion of a Q-wave, while Q is definite in Lead II. Since S_3 is preceded by no R, it would be interpreted as a deep Q-wave according to Pardee. The terminal portion of R_1 and R_2 shows splintering. QRS width is normal. R-T interval is below isoelectric level in Lead I, above it in Lead III. Still from our own experience we would prefer not to consider this record indicative of recent coronary thrombosis but to compare it with Fig. 1 as an expression of left axis deviation. Rather it seems to us that the appearance of Q_2 indicates old infarction on the posterior wall of the heart. Fig. 14*b* is a record taken with the oscillometer three days before death. It shows fundamental changes in all leads. The high waves have been replaced by deflections of very low voltage. Q_1 and Q_2 persist. The rudimentary R_1 still shows the terminal splintering; R_2 has likewise almost disappeared, but its terminal part retains the same form. In Lead III the deep S or Q is replaced by a little *W*. R-T in Lead I now shows definite elevation above the isoelectric level, while S-T is depressed in the third lead.

Summary. Old thrombosis of the circumflex and recent thrombosis of the anterior descending ramus with localized areas of malacia. While the electrocardiogram before the second attack showed left axis deviation with high voltage, after the closure of the anterior descending ramus a marked reduction of all waves gave the picture of low voltage. Certain portions of the curve remained unaltered.

We find a similar case in Levine's paper. In Fig. 29, taken three days after closure, there is marked left axis deviation. From the fourth to the eighth day this yields to low voltage through a lowering of R_1, R_2, and S_3. The form of the waves is retained. On the tenth day the original form reappears. This differs from our case in that

there is certainly a disturbance of intraventricular conduction (according to Levine in the right branch?). Then on the seventh day the small and normal complexes alternated, according to either a lengthening of the recovery time (normal waves) or a shortening of conduction (small waves). In the same group belongs a case described by Cooksey and Freund[17] which at autopsy showed an old, partially canalized thrombus of the right coronary artery and a recent closure of the anterior descending ramus with a large infarct of the anterior wall of the left ventricle (Fig. 14 *c* and *d*).

COMMENT

If we assemble the essential facts of the three groups, we find the following results. In the first group are reported 7 of our own cases and 19 cases from the literature. In all which came to autopsy the diagnosis of coronary closure was verified, invariably affecting the left ventricle and, where noted, the anterior descending ramus. The diagnosis in those cases which did not come to autopsy was established on clinical and electrocardiographic evidence. The characteristic common to all is the change in the initial complex of the electrocardiogram. In Lead I there is a small R-wave, while S is absent or rudimentary, and Q may be present or absent. Leads II and III are dominated by a deep S-wave which is greater than any of the other waves of any lead. The preexisting electrocardiogram usually showed left axis deviation. The changes may appear immediately or some time after the attack, may persist or disappear, usually last longer than do the changes of the final complex. We shall indicate the changes of this group by the abbreviation "*aBB*," by which we mean that *a* is an upward and *B* a downward deflection of the initial complex and that *a* is a small and *A*, a large deflection.

The second group, which for convenience we shall indicate as b_{1-3}, includes seven of our own and five cases from the literature. Two of the former and four of the latter cases were verified post mortem, and in the others severe myomalacia was recognized clinically. In the autopsied cases the anterior descending ramus and the region supplied by it were invariably affected. In this group the electrocardiogram is characterized by the negativity of the principal deflections in all leads. Usually, too, the waves are smaller than normal. The main deflection may be a Q or an S. In the observed cases the electrocardiographic changes appeared only after an interval and persisted. In Levine's Case 44 the R_1 became greater than S_1 nine months after the attack.

The third group is made up of one case which we verified at autopsy and two cases from the literature. The two cases which were examined post mortem showed old thrombosis,—once of the right, once

of the circumflex branch of the left coronary artery—and a recent closure of the anterior descending ramus with resulting infarction. The electrocardiographic changes first appeared after the second closure. Before this attack the electrocardiogram showed left axis deviation with high waves; immediately after this attack there was a prompt decrease in the size of the principal waves in all leads, while smaller deflections retained their characteristic form. The result of these changes is an electrocardiogram with low, slurred and notched waves similar to that described by Oppenheimer and Rothschild[7] as indicating arborization block. A real widening of the QRS group was found only in Levine's case (see Fig. 29 of his monograph) where there was evidence of definite interference with intraventricular conduction. In this case the electrocardiographic changes persisted for a few days only; in the other cases they lasted to death, which occurred rather promptly. The characteristic of this group is not so much the electrocardiographic picture after the insult as the promptness with which successive changes appear. These cases will escape observation if they are not followed closely as the changes develop.

DISCUSSION

Practically the most important question is whether the changes are pathognomonic so that on their appearance alone one is warranted in making a diagnosis of coronary closure and infarction of the heart. The close association between the changes in the ventricular complexes, the time of infarction and the autopsy findings makes it appear certain that the changes in the initial complex are the result of, and not merely coincidental with, the myocardial changes. Still it is not certain that similar electrocardiographic changes might not occur in other conditions. This possibility cannot be excluded for the end-picture of the third group, for this picture is not sufficiently clear cut. For the pictures of groups one and two we can say, on the basis of clinical experience which is founded on the examination of over 10,000 electrocardiograms at the First Medical German Clinic, that they are certainly uncommon; indeed those of group two (b_{1-3}) are distinctly rare. Particularly in oscillograph electrocardiograms, the appearance of pronounced S-waves is definitely abnormal. In cases of ordinary left or right axis deviation the appearance of S-waves in all leads does not occur. To secure objective evidence on this matter we looked through 1,460 electrocardiograms from different individuals chosen at random from our files and for the most part derived from patients with abnormal hearts. We examined these tracings to select those which showed the following features: (1) electrocardiograms in which S_2 and S_3 were greater than the R-wave of any lead in which R_1 was greater than S_1, and (2) electrocardiograms in which the principal

deflection was downward in all leads, regardless of whether this deflection was an S or a Q. Of the first group we found 19 cases (1.3 per cent) of which four are included in this report; five others probably had myocardial infarct; two lacked clinical data; and seven gave no evidence for a diagnosis of infarction of the heart. Yet it must be noted that of the seven apparently contradictory cases six differed from our Type aBB in that they showed very low voltage, with S_2 and S_3 smaller than 6 mm. Of the second group we collected eight cases (0.55 per cent) of which four are considered in this study, and two others are suggestive of myocardial infarct; one case lacks clinical data and only one case (congenital anomaly) seems contradictory. Cases of third degree automatism were not included. From these results we conclude that the appearance of an electrocardiogram of Type aBB or of Type b_{1-3} is strongly suggestive, if not absolutely pathognomonic, of myocardial infarct. The same indeed may be said for the "coronary T-wave"; the sharply inverted T and the plateau T may be found in other conditions. Increase in the size of Q_3 can be interpreted only with reservations. While, according to Freundlich,[11] the "coronary Q-wave" is always associated with changes in the final complex, the changes in the initial complex which we have described are independent of other electrocardiographic findings, a fact which enhances their clinical value. Levine noted that the cases reproduced in our Fig. 8 *c* and *d* showed nothing unusual. Also we find the initial complex to be the only evidence pointing to infarction in Figs. 6*a* and 12*a*. It seems probable that *more attention directed to the initial complex will reduce the number of cases hitherto classed as silent coronary thrombosis.* The changes which we have described resemble the other recognized electrocardiographic criteria for the diagnosis of coronary thrombosis in significance but not in frequency.

It is not clear why only a fraction of the cases of true coronary thrombosis shows the changes described in the QRS complex. Two possibilities must be considered. In the first place it is only natural that the form of the electrocardiogram before the insult should influence its further development. In most of the cases cited the preexisting electrocardiogram showed left axis deviation with fairly high waves as nearly as can be determined. How the QRS changes would manifest themselves if, before the insult, there was right axis deviation or some other type of record, must be determined by further studies. Exceptionally, however, changes of Type aBB or b_{1-3} may appear without earlier left preponderance, as Fig. 11 shows.

The second factor which influences the appearance or absence of changes in the initial complex is the localization and extent of the infarct. It cannot be an accident that all the autopsy protocols showed evidence of infarction of the left ventricle, usually with extensive

myomalacia in the area supplied by the anterior descending ramus. One might object that this localization is the most common one, not only in the cases cited here, but generally. However, if one accepts the statement of Levine, who has most data on this point, that 85 per cent of the cases of coronary thrombosis involve the anterior descending ramus, one would expect from the number of our cases that now and again the thrombosis would have a different site. This is not the case in either group one or group two, whereas in both the autopsied cases of group three there was double thrombosis. On other grounds it appears to us not improbable that different anatomical processes underlie the first two and the third groups. But this argument is not sufficient to explain the absence of the changes in the initial complex in a series of cases. Fig. 7 of Levine's monograph shows clear left axis deviation which remained until death in spite of the fact that autopsy showed an extensive infarct of the anterior wall of the left ventricle.

In an attempt to explain the mechanism underlying the formation of changes in the initial complex after cardiac infarction, we are aware that we enter upon the uncertain territory of theory. We can with certainty exclude the possibility that extracardiac factors, such as change in the position of the heart or altered peripheral resistance, have anything to do with the process. There remain therefore only two other possibilities. Either the changes are the expression of a definite disturbance of intraventricular conduction, or they are the reflection of a change in the dynamic balance of the two halves of the heart.

1. *Theory of disturbance of conduction.* Certainly neither the electrocardiogram of Type aBB nor that of Type b_{1-3} corresponds with the familiar picture of arborization or bundle-branch block. At first glance it might seem that Type aBB could be considered as a modification of the usual form of bundle-branch block (so-called right bundle-branch block). The assumption of a block situated so high is incompatible with the anatomical localization; since usually it is only the lowest part of the intraventricular septum which is involved in the necrosis. For the acceptance of intraventricular or bundle-branch block one requires a delay in intraventricular conduction time, and for a disturbance of both branches one must have a prolongation of the P-R interval. Such a condition was present only once in all our material. As to the increased duration of QRS as the expression of a delay in the spread of the excitatory process through the ventricles, the following table shows the results found in our cases. In Table I is shown the greatest duration of the initial complex in any one of the three usual leads.

TABLE I

THE GREATEST WIDTH OF THE INITIAL COMPLEX IN ANY LEAD OF THE ELECTROCARDIOGRAM

CASE	BEFORE ONSET OF QRS CHANGES	DURING PERIOD OF CHANGES	AFTER RECOVERY
Type aBB			
Case 1	–	0.105	0.12
2	–	0.10	–
3	0.12	0.115	–
4	–	0.09	0.08
5	0.095	0.095	–
6	–	0.12	–
7	–	0.08	–
Levine, 1	–	0.10	–
8	0.06	0.08	–
17	–	0.10	–
30	–	0.095	–
43	–	0.095	–
76	–	0.10	–
77	–	0.115	–
Dressler	–	0.10	–
Freundlich, 11	–	0.09	–
12	–	0.095	–
Mahaim	–	0.10	–
Condorelli	–	0.10	–
Oettinger	0.08	0.10	–
Type b_{1-3}			
Case 8	–	0.08	–
9	–	0.09	–
10	0.07	0.07	–
11	–	0.09	–
12	–	0.09	–
13	–	0.08	–
14	–	0.113	–
Levine, 36	–	0.075	–
44	–	0.085	–
Type c_{1-3}			
Case 15	0.12	0.10	–
Levine, 29	0.10	0.13	0.10
Cooksey	0.11	0.08	–

Two things must be considered in interpreting these figures. It is possible that the widening of the initial complex is dependent on a preexisting and unrelated bundle-branch disturbance, as in Cases 3 and 15 in which before the onset of the coronary thrombosis the initial complex was widened to a duration of 0.12 sec. On the other hand, the degree of widening of the QRS complexes which is found in Table I is not definite proof of interruption of the path of conduction through a bundle branch, for we may find such slight change in cases of marked hypertrophy.[18] If, in our series of 31 cases, we find the duration of QRS to be less than 0.1 sec. in sixteen cases, just 0.1 sec. in nine, and more than 0.1 in seven, we are certainly not justified in drawing any conclusions as to the importance of widening of QRS as one of the criteria of the changes in the initial complex or as to the existence of a disturbance of conduction in all these cases.

Histological studies of the conducting fibers of appropriate cases would be of help in solving the problem. Unfortunately we did not make serial sections of our cases, nor does Levine's material have this information. Only in Mahaim's[8] case were there satisfactory histological studies. As a matter of fact examination of his case (see our Fig. 10*d*) showed complete interruption of the right branch and partial destruction of the left. He attributed the electrocardiographic changes to this lesion of the conducting system. We do not feel that we can draw final conclusions from this isolated case, especially as the P-R interval was normal as opposed to the histological picture.

Regarding the great difficulty in making, and the caution required in interpreting, histological studies of the heart, we refer to the judgment of such experienced investigators as Lewis.[19] Even regarding the laborious and precise studies of Mahaim some doubt arises. In the case in question the cause of the infarct is given as a septic embolism occurring in the presence of open foramen ovale, which seems incompatible with the history of increasing decompensation for one year as well as with the macroscopic picture of the usual ventricular aneurysm with adherent pericardium but no evidence of infection. Elsewhere in Mahaim's work doubt arises over the agreement of histological findings with incorrect electrocardiographic diagnoses. Thus on page 169 in a case of ventricular rhythm in complete block he interprets the form of the beats arising in the ventricle to a coexisting bundle-branch block which seems quite unlikely. Moreover, the histological picture is opposed to the diagnosis of bundle-branch block. In Fig. 30 (p. 120) he shows an illustration of complete block in which the auricular rate is somewhat less than twice the ventricular rate and calls it "Type II, 2:1 rhythm" which is quite erroneous.

One must wait for further evidence before interpreting Type aBB as a special form of intraventricular block. This interpretation is still less probable as applied to Type b_{1-3}, for we find that eight of the nine reported cases have a QRS duration which is normal. The possibility of disturbance of conduction in the terminal ramifications of the right bundle cannot be affirmed or denied since we know little of this condition in animals and nothing of it in man. Wilson and Herrmann,[20] on the bases of experiments with dogs, doubt that lesions of the terminal ramifications lead to substantial electrocardiographic changes.

2. *Theory of disturbed muscular balance.* This rests on the assumption that the mass of muscle which is cut off from the circulation by the closure of a vessel no longer gives rise to a process of electrical activity. This must lead to a change in the dynamic relation between the right and the left sides of the heart and to a distortion of the original ventricular complexes. It is easy to understand that an infarct of the left ventricle would lead not only to a decrease in the left axis deviation, but also to unusual modifications of the waves, for it is only a part of the left ventricle which is cut out; the potential of the remaining part is not disturbed. The fact that the appearance of the changes which we described in the initial complex was linked with a

large infarct supports this interpretation. It is more difficult to understand why in some cases the changes in the initial complex following coronary closure may be delayed considerably, and in a few cases they are reversible. We must remember that the development of necrosis is not always acute, nor is the process in the vessels always linked with the acute syndrome of coronary occlusion. Again there may be some return of circulation in the affected area either through a collateral circulation or through canalization, particularly when the general circulation improves with a rise of pressure in the aorta. The autopsy findings in the third group of cases fit in with this idea, for here the electrocardiogram showed simple decrease in the waves, while a double thrombosis had cut out a large part of the two sides of the heart. Our interpretation fits in with the opinion expressed by Hahn[21] who in the case of a patient with a history of hypertension saw the axis deviation change from left to right after the second infarct, and who expressed the possibility that this was a result of change in the dynamic equilibrium following the infarct.

It would be pleasant to try to determine in the case of Type aBB and especially in the case of Type b_{1-3} how the electrical axis changes in the individual phases of the electrocardiogram with the appearance of changes in the initial complex. Apart from the fact that very recently serious objections have been raised to the older methods of determining axis deviation, our apparatus is, unfortunately, not set up to register two simultaneous tracings.

SUMMARY

Fifteen personal cases and 26 from the literature are reported, in which characteristic changes appeared in the initial complex following a coronary closure. These changes appeared immediately or some time after the insult, and remained definite or regressed.

The changes may be classed in three groups. In the first, one finds a modified form of left axis deviation with small R_1 and deep S_2 and S_3. The characteristic of group two is the negativity of the principal deflection of all leads, whether this be S or Q. The third group is recognized by the shrinking of all the main waves while smaller deflections may persist unchanged.

The anatomical basis for the first two groups is an extensive necrosis of the anterior heart wall; for the third group it is necrosis of anterior and posterior walls as a result of two thromboses. Controlled by a series of 1,460 electrocardiograms chosen at random, these changes were found to be not pathognomonic, but most suggestive of the presence of infarct of the heart. They occur less frequently than do the hitherto recognized signs of coronary thrombosis, but they may be present in those cases in which there are no characteristic changes in the final complex.

As the interpretation of the QRS changes, a disturbance of the muscular balance of the two sides of the heart caused by the cutting out of a large mass of muscle is brought forward, but the possibility remains that for each group there is a localized disturbance of intraventricular conduction.

Later Note. While we were writing our paper, a work by Wilson, McLeod, Barker, Johnston and Klostermeyer (Heart **16**: 155, June 1933) first came to our attention, at a time when our observations were already complete. These writers also studied changes in the QRS complex after coronary thrombosis and listed two types which they indicated as Type Q_1 and Type Q_3. The first of these has in addition to Q_1 a very small R_1 and a deep S_2 and S_3. Thus in Figs. 1, 2, 4 and 8 we recognize our Type aBB, in Figs. 2, 5 and 19 our Type b_{1-3}. Our third type is also shown twice, once with sure signs of intraventricular block, and once without this. The autopsy findings correspond to those of our cases. The authors place most emphasis on the Q changes but must add that the Q_1 type may occur without Q_1 as the single illustration evidences. The Q_3 type has nothing to do with the cases which we have described and at present seems to us not very characteristic. Concerning the relation between the electrocardiographic picture and the site and extent of the infarction, we feel that the authors are too cautious. Also they incline to the view that the changes in the initial complex are an expression of the cutting out of the infarcted part of the muscle.

REFERENCES

1. Herrick, J. B.: J. A. M. A. **81**: 387, 1919.
2. Smith, F. M.: Arch. Int. Med. **22**: 8, 1918.
3. Pardee, H. E. B.: Arch. Int. Med. **26**: 244, 1920.
4. Wearn, J. T.: Am. J. M. Sc. **165**: 250, 1923.
5. Wilson, W. J.: Ann. Clin. Med. **5**: 238, 1926.
6. Fenichel and Kugell: Am. Heart J. **7**: 235, 1931.
7. Oppenheimer and Rothschild: J. A. M. A. **69**: 429, 1914.
8. Mahaim, I.: Les maladies organiques du faisceau de His-Tawara, Paris, 1931, Masson et Cie.
9. Edeiken and Wolferth: Am. Heart J. **7**: 695, 1932.
10. Ziskin, T.: Arch. Int. Med. **50**: 435, 1932.
11. Freundlich, I.: Deutsches Arch. f. klin. Med. **175**: 129, 1933.
12. Levine, S. A.: Coronary Thrombosis, Baltimore, 1929, Williams & Wilkins.
13. Dressler: Atlas der klinischen Elektrokardiographie, Tafel VII, Abb. 22, Berlin and Wien, 1933, Urban & Schwarzenberg.
14. Condorelli, L.: Die Ernährung des Herzens und die Folgen ihrer Störung, Dresden, 1932, Theodor Steinkopff.
15. Smith, F. M.: Arch. Int. Med. **32**: 503, 1923.
16. Oettinger, I.: Ztschr. f. klin. Med. **175**: 129, 1933.
17. Cooksey and Freund: Am. Heart J. **6**: 608, 1931.
18. Wenckebach and Winterberg: Die unregelmässige Herztätigkeit, Wien, 1927, p. 347, Wilhelm Engelmann.
19. Lewis, T.: The Mechanism and Graphic Registration of the Heart Beat, London, 1925, p. 182 ff., Shaw & Sons, Ltd.
20. Wilson, F. N., and Herrmann, G. R.: Arch. Int. Med. **26**: 153, 1920.
21. Hahn, L.: Ztschr. f. Kreislauf. **25**: 369, 1933.
22. Koch, Elsb: Ztschr. f. Kreislauf. **25**: 513, 1933.

THE DURATION OF THE QRS COMPLEX IN THE NORMAL AND IN THE ABNORMAL ELECTROCARDIOGRAM

A Study of 500 Cases, With a Note on Nomenclature*†‡

Sylvester McGinn, M.D., and Paul D. White, M.D.
Boston, Mass.

A SURVEY of the literature has failed to reveal sufficient statistical data to establish durations for the QRS complexes of the normal human electrocardiogram at all ages, although 0.1 second as the upper limit has been set by common experience. The question has recently been asked whether or not this figure is higher than it should be. Hence we have made accurate measurements of the duration of the initial ventricular complexes in all leads in a series of 500 individuals, of whom 150 were normal and 350 had heart disease. In connection with this study several points of related interest have come to our attention.

LITERATURE

(a) *Normal Individuals.* A number of the standards employed in reading electrocardiograms originated in the earliest days of electrocardiography from the work of Lewis and Gilder[8] which consisted of an analysis of the tracings of 52 normal males between the ages of eighteen and thirty-five years. The duration of the QRS complex was not considered at that time; but in a subsequent study by Lewis, among other determinations, the average duration of this complex for eight normal individuals was estimated to be 0.0784 second. In his book, *The Mechanism and Graphic Registration of the Heart Beat,* Lewis[7] states in referring to the QRS group of deflections, "This group of deflections has a total duration of no more than 0.1 of a second, and usually constitutes less than one-third of the full ventricular complex." Again in another passage he says, "the QRS group of the normal human electrocardiogram lasts 0.08 of a second in the average." Ferguson and O'Connell[2] reported that in the electrocardiograms of 1,812 young men without symptoms referable to the heart only two had QRS durations of over 0.10 second. Jensen, Smith, and Cartwright[4] found the duration of the QRS complexes to be between 0.06 and 0.08 second in a majority of 50 patients between the ages of fifty and sixty-five years.

*From the Cardiac Clinics and Electrocardiographic Laboratory of the Massachusetts General Hospital.

†Presented by title before the American Society for Clinical Investigation, Atlantic City, May 2, 1932.

‡The tables will be published in the reprints of this article. A copy of the reprint may be obtained by writing to the authors.

The electrocardiograms of normal children have been studied more extensively than those of adults. Scham[10] in his section devoted to electrocardiography in Abt's *Pediatrics* gives the duration of the QRS complex as 0.036 second in normal infants eleven days to one year of age; 0.049 second in children one to five years of age; and 0.069 second in the later years of childhood. Lincoln and Nicolson[9] found the average duration of the QRS complex to be 0.06 second as observed in the electrocardiograms of 222 normal school children between the ages of three and twelve years.

(b) *Patients With Heart Disease.* Lewis[6] has reported measurements of the duration of the QRS complex in a few abnormal electrocardiograms. It was found to average 0.1005 in six curves with "left ventricular preponderance" and 0.0788 in six having right axis deviation consequent to mitral stenosis. He believed that the reasons for this difference are that there is a greater increase in the total muscle mass in left ventricular hypertrophy and that the end phases of the complex represent the spread of the waves in the left ventricular wall. Fahr[1] found that the QRS complexes of electrocardiograms of pure left ventricular enlargement were more prolonged than were those in normal curves and measured from 0.10 to 0.12 second. He attributed this prolongation to the increased length of the conduction path in the hypertrophied muscle through which the impulse must travel.

Wilson and Herrmann[11] have considered that a relationship exists between the duration of the QRS complex and the ventricular weight, but that when the measurement exceeds 0.10 second, some factor other than hypertrophy of the muscle is responsible, such as defects in the intraventricular conducting system.

PRESENT STUDY

We have studied a series of 500 electrocardiograms in which the QRS complexes of all three classical leads have been measured by means of the Lucas comparator. We have included in this series the tracings of 100 normal adults, 50 male and 50 female, and of 50 normal children twelve years of age and under. These individuals have been examined by us and have shown no evidence of cardiac disease. The remaining 350 electrocardiograms are representative of various cardiac disturbances and consist of 100 having abnormal left axis deviation, 50 of which have upright T-waves in Lead I, and 50 inverted T-waves in Lead I; 50 with abnormal right axis deviation; 50 with normal T-waves but from patients having heart disease, 50 with abnormal T-waves from patients having heart disease; 50 with intraventricular block of lesser grades; 30 with bundle-branch block, of which 20 show left axis deviation and 10 right axis deviation; and 20 cases of premature beats, of which 10 are of ventricular origin and 10 of auricular origin. The ectopic complexes show

right axis deviation in 5 of the electrocardiograms with ventricular premature beats and in the other 5 left axis deviation. Of the 10 tracings having auricular premature beats the abnormal P-waves are followed by normally shaped ventricular responses in 5 and by some degree of aberration of the ventricular responses in the other five.

Our procedure has been to measure three QRS complexes in each of the three leads by means of the Lucas comparator. The average duration of the complexes of each separate lead was estimated, and the largest of the three figures was taken as representing the maximum duration of the ventricular complex for that electrocardiogram. Simultaneous records in which Leads I and II and Leads III and I were taken together form a part of the total 500 tracings. All the electrocardiograms were standardized (one millivolt equals one centimeter) and none showing instrumental artefacts, such as overshooting, were included in the study.

The Lucas comparator has been described in detail by Lewis.[5] It includes a microscope at each end of a movable bar, one of which is directed on the electrocardiogram and the other on a scale so graduated that readings are possible to one-hundredth of a millimeter. The computation of the measurements includes corrections for variance in the time marker by using percentages which automatically check themselves. The figures are translated into time relations so that the final answer as to the duration of the QRS complex is given in fractions of a second.

Lewis found that the possible error for this type of calculation in measuring R-R intervals was 0.0234 second for the maximum, but that the greatest variation more closely approached the minimum possible error of 0.0028 second. To insure as much accuracy as possible the measurements of 250 of our series of 500 electrocardiographic records were remeasured and compared with the first readings. The difference with very few exceptions amounted to only a few hundredths of a millimeter and depended upon the determination of the end points by two individuals.

FINDINGS

Normal Adults. The average duration of the QRS complex in the electrocardiograms of our series of 100 normal adults of all ages (see tables in reprints) was 0.0777 second. Half this group of patients were males who had an average duration of the QRS deflection of 0.0833 second; 66 per cent of these males had a QRS duration longer than 0.0800 second. The 50 females had shorter duration times of the QRS complex than did the males. The average for this group was 0.0722 second with only 20 per cent over 0.0800 second. The width of the QRS waves had no consistent relationship to the ages of these 100 normal adults, to their pulse rates, or to the amplitudes of their ventricular complexes. Of the 50 normal male patients 11 were tall in stature, 10

of whom had QRS complexes wider than 0.0833 second, the average for the group. One tall patient was included in the group of 50 normal females, and she had a duration time of 0.0782 second. The widths of the QRS complexes in patients considered to be overweight were below the average for the group as frequently as they were above it.

The longest QRS times were most frequently observed in Lead III; this was true in 44 tracings. The duration of the QRS complex was the most prolonged in Lead II in 37 electrocardiograms and in Lead I in 19 instances. In the electrocardiograms of 16 of the normal adults, Leads I and II and Leads III and I were taken simultaneously; the widest QRS wave was found in Lead III in 9 of these individuals.

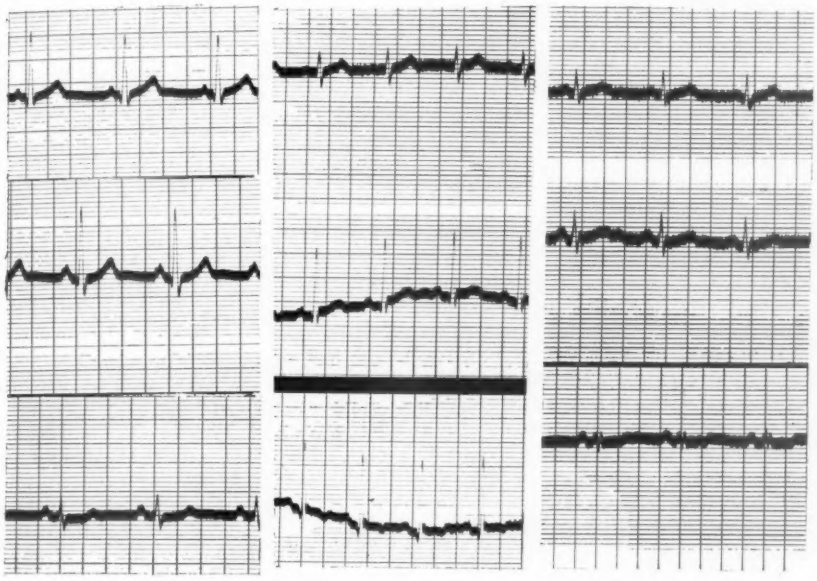


Fig. 1.—Electrocardiograms of normal individuals. *A*, Common type with the usual QRS complex; *B*, widening of the QRS in Lead III due to an upright S-wave (Leads I and II recorded simultaneously); *C*, widening of the QRS due to notching in Leads II and III (Leads I and II recorded simultaneously); the voltage of the QRS waves in this record is rather low.
Leads I, II, and III are shown in order in these records and in those of the figures to follow. Time interval 0.2 second. Amplitude 1 mm. 10^{-4} volt.

In 18 of the 100 normal adults' electrocardiograms the QRS duration was more than 0.0900 second. The majority of these records showed individual variations in the ventricular complexes that accounted for the prolongation. Slurring of the descending limb of the R-wave and notching of the QRS in Lead III were found frequently. Three of these 18 tracings had a duration of the QRS wave greater than 0.100 second; 2 of these 3 had in Lead III low voltage and considerable notching of the ventricular complexes. An "upright S-wave" superimposed on the descending limb of the R-wave in Lead III was found in three

tracings and an "upright Q-wave" was found interrupting the ascending phase of the R-wave in Lead I in another electrocardiogram.

Normal Children. The electrocardiograms of 50 normal children twelve years of age and under were studied to determine the duration of the QRS complex in childhood. It was found to average 0.0719 second, very closely approximating the average measurement found in the 50 normal females and somewhat longer than has been previously reported for children. There were 26 boys and 24 girls in this series, the former tending to have slightly wider QRS complexes than the latter. Of 28 cases in which the duration of the ventricular complex was more than 0.0700 second, 18 were boys. The youngest children were included in the group whose tracings showed the QRS duration to be 0.0700 second or less, the average age being 7.4 years as compared with 8.3 years for the group with QRS durations longer than 0.0700 second. The ages of the children were as follows: two years 4 children, three years 1, four years 1, five years 2, six years 8, seven years 4, eight years 5, nine years 7, ten years 7, eleven years 6, and twelve years 5.

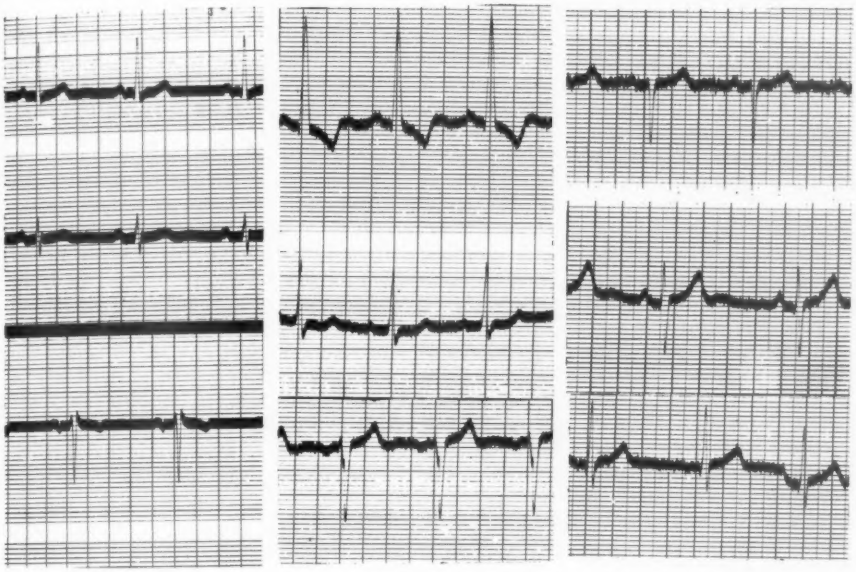
ABNORMAL CASES

Abnormal Left and Right Axis Deviation. The duration of the QRS complex was determined in 100 electrocardiograms having an abnormal degree of left axis deviation; 50 of these had upright T-waves in Lead I and the other 50 inverted T-waves in Lead I. In the 50 cases with upright T-waves in Lead I the QRS wave had an average duration of 0.0889 second; Lead III was completely inverted in 14 of these cases (in 8 of these the QRS wave duration exceeded the average for the group of 50). The electrocardiograms of this first group of 50 cases were obtained from 30 males and 20 females; of the latter only 4 had QRS complex durations greater than the general average of 0.0889 second for the 50 cases. The maximum duration of the ventricular complex was found in Lead III 19 times, in Lead II 17 times, and in Lead I 14 times. There were 36 tracings with simultaneous records of Leads I and II and of Leads III and I. In these special films the QRS complex was widest in Lead III fifteen times and in Leads II and I twelve and nine times respectively.

The average duration of the QRS wave in the 50 cases having an abnormal degree of left axis deviation and an inverted T-wave in Lead I was 0.0985 second. Lead III was completely inverted in 6 of these 50 electrocardiograms, of which number 2 had QRS waves wider than the average for the group. There were tracings from 36 male patients and 14 female patients. Nine of the female patients had QRS waves wider than 0.0985 second which was the average for these 50 patients. The widest QRS wave was recorded in Lead III in 21 instances, in Lead II in 11, and in Lead I in 18. There were 20 electrocardiograms in

which two leads were taken simultaneously, and it was shown that the widest QRS wave appeared seven times in Leads II and III respectively and 6 times in Lead I.

Fifty electrocardiograms having an abnormal degree of right axis deviation were measured, and in these the average duration of the QRS complex was found to be 0.0870 second. Equal numbers of males and females were represented in this series and were evenly distributed in relation to the average duration of the QRS wave for the group. The widest QRS complex was found 23 times each in Leads II and III and only 4 times in Lead I. In 13 electrocardiograms with leads taken simultaneously, the greatest duration of the QRS complex was found in Lead



A *B* *C*

Fig. 2.—Electrocardiograms with abnormal axis deviation. *A*, Left axis deviation with upright T-wave in Lead I (Leads I and II recorded simultaneously); *B*, left axis deviation with inverted T-wave in Lead I (Leads I and II recorded simultaneously); *C*, right axis deviation.

III five times, in Lead II six times, and in Lead I twice. Eleven of the patients whose electrocardiograms showed an abnormal degree of right axis deviation had congenital heart disease and the others, with two exceptions, had mitral stenosis. Nine of the patients with congenital heart disease had QRS complexes wider than 0.0800 second.

A comparison of the above three groups of electrocardiograms (each group containing 50 electrocardiograms) indicates that the average duration of the QRS complex is longest in the records having abnormal left axis deviation with inverted T-waves in Lead I. The average durations of the QRS waves in those tracings having abnormal left axis deviation with upright T-waves in Lead I and

those with abnormal right axis deviation were similar, and more closely approached that found for normal adults although still exceeding it somewhat.

Electrocardiograms of 100 Patients With Heart Disease Without Any Abnormal Degree of Either Left or Right Axis Deviation. The electrocardiograms of 100 patients with heart disease without any abnormal degree of either left or right axis deviation were studied, and the duration of their QRS complexes was determined. There was no bundle-branch block in these tracings. In 50 of the 100 cases there were abnormal T-waves in Lead I or Lead II, and in 50 there were no abnormal T-waves in either Lead I or Lead II.

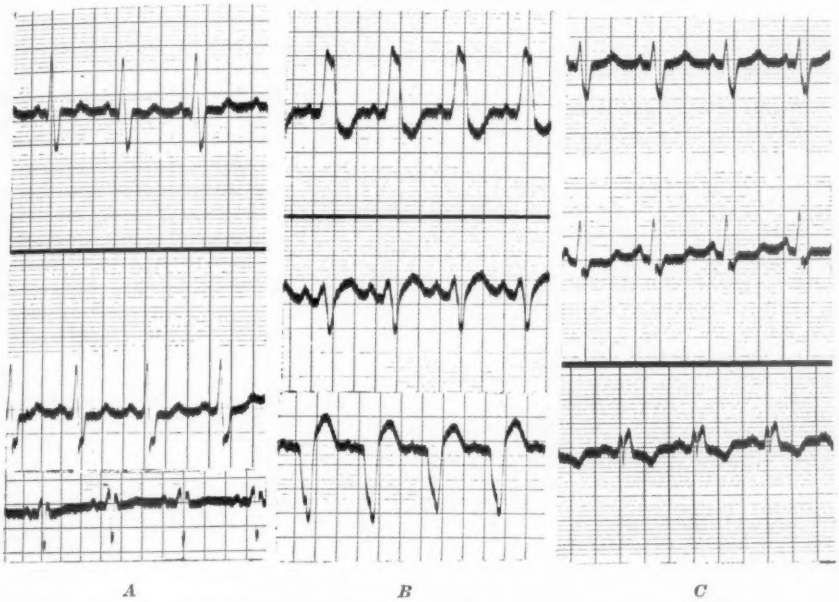
All the 50 electrocardiograms in which the T-wave was upright in Leads I and II were those of patients in whom we had made the diagnosis of undoubted angina pectoris, 42 of their number being males. The average duration of the QRS complexes in these 50 cases was 0.0779 second. Twenty-two of the 50 records showed the widest QRS complexes in Lead II, 17 in Lead III, and 11 in Lead I. Four of the 7 films in which the leads were taken simultaneously showed the widest QRS complexes in Lead I.

The average duration of the QRS complex was 0.0827 second in the 50 electrocardiograms of patients having heart disease and abnormal T-waves in Lead I, in Lead II, or in both Leads I and II, but in which there was neither abnormal axis deviation nor bundle-branch block. The diagnosis of coronary thrombosis was made by us clinically in all these 50 patients. There were 21 tracings with an inverted T-wave in Lead I and 14 with a diphasic T-wave in Lead I. Of the remaining 15 electrocardiograms 10 had an inversion of the T-wave in Lead II and 5 had diphasic T-waves in Lead II. Six of the 10 electrocardiograms having inverted T-waves in Lead II had QRS wave durations of over 0.0900 second; otherwise there was no suggestive relationship between the width of the QRS complex and the type of T-wave. Forty-four of these 50 electrocardiograms were from male patients. The widest QRS complexes were found 21 times each in Leads I and II. There were 17 tracings in which two leads were taken simultaneously, and of this number the QRS wave was widest in Lead II in the majority of instances.

Intraventricular Block Including Full Bundle-Branch Block. The ventricular complexes were studied in 50 electrocardiograms showing the presence of intraventricular block of slight to moderate degrees (not the full classical bundle-branch block) and in 30 electrocardiograms showing full bundle-branch block. The average duration of the QRS waves in the first group was 0.1307 second with the two extremes 0.1007 second and 0.1640 second. There were 46 males and 4 females represented in this group of 50 patients; two of the 50 patients complained of diseases not related to the heart, two had functional cardiac dis-

turbances,* and the remainder had complaints due to organic heart disease. The widest QRS complex was found in Lead III in 19 tracings, in Lead II in 18, and in Lead I in 13. Of 10 electrocardiograms with two leads taken simultaneously, the duration of the QRS complex was greatest in Lead III on 6 occasions.

Three additional electrocardiograms were measured in which the interpretation had been intraventricular block on account of the shapes of the QRS waves, although the duration of the ventricular complex was less than 0.100 second. The measurements of the durations of the QRS waves in these cases were 0.0896 second, 0.0931 second, and 0.0996 second respectively. It is thought that the interpretation of intraventricu-



A *B* *C*

Fig. 3.—Electrocardiograms showing defects in the ventricular conducting system. *A*, Intraventricular block of lesser degree; *B*, bundle-branch block with left axis deviation; *C*, bundle-branch block with right axis deviation (Leads I and II recorded simultaneously).

lar block was justified because of the extreme notching and altered shape of the ventricular complexes despite their relatively short durations.

The durations of the ventricular complexes were estimated in 30 electrocardiograms having typical bundle-branch block, of which number 20 had left axis deviation and 10 right axis deviation. The former under the old terminology are considered to indicate defects in the

*An electrocardiogram was studied representative of the group of cases reported by Wolff, Parkinson, and White[12] in which there were sometimes widened QRS waves with short PR intervals and at other times normal complexes with PR intervals of usual length. Two complexes of each type were measured, and the intervals from the beginnings of the P-waves to the ends of the S-waves were found to be approximately the same (0.22 second and 0.21 second respectively). This is evidence supporting the suggestion by Holzmann and Scherf[3] that in these cases there may be a special conduction tract between auricles and one or the other ventricle in addition to the A-V node and the bundle of His.

right branch of the bundle, but left bundle-branch block according to the new nomenclature. Lewis found that the average duration of the QRS complex in 7 tracings having such changes was 0.1396 second; in our 20 cases it was 0.1499 second. Twelve of the 20 patients were males. The majority of these 20 records showed the widest QRS waves in Lead II.

The 10 tracings having bundle-branch block with right axis deviation gave an average duration of the QRS complex of 0.1412 second. Six of these patients were males. The widest QRS complexes were most often found in Lead III in this group.

Ventricular and Auricular Premature Beats. Twenty electrocardiograms having frequent premature beats were studied, and the durations of the first ventricular complexes (QRS waves) were determined. It was not possible to obtain 3 of these special complexes in every lead for measurement as had been the procedure throughout the series; however, no fewer than 7 premature beats were measured in each instance.

The average duration of the QRS waves of ventricular premature beats with left axis deviation was 0.1374 second in 5 electrocardiograms. Three of these patients were males. The duration of the QRS waves of ventricular premature beats having right axis deviation was 0.1401 second in 5 electrocardiograms of 5 other cases. Those ventricular complexes having the longest time intervals were found most frequently in Lead III.

The normal ventricular responses to auricular premature beats were measured in 5 electrocardiograms, and the average width of the QRS waves was found to be 0.0801 second. There were four males and one female represented by these electrocardiograms. The widest QRS complexes were found twice in Lead II and twice in Lead III. In five other electrocardiograms the duration of the QRS wave was determined for aberrant ventricular responses to auricular premature beats. The average duration of these QRS intervals was 0.1216 second. Three of the tracings were from male patients. The greatest aberration of the ventricular responses to ectopic auricular beats was observed twice in Lead I and twice in Lead II.

NOTE ON NOMENCLATURE

The present study has called our attention to the inconsistencies of the nomenclature of the QRS complex of the electrocardiogram. In describing the ventricular complex the method most in vogue at the present time of calling the upward deflection of the QRS complex the R-wave and the downward deflections Q and S according as they precede or follow the R-wave is unsatisfactory in that there may be more than one upward deflection (see Lead III of Fig. 4*A*) and in that the first downward deflection may be deep and wide, not in appearance like the usual

Q-wave and in time coincident with the R-wave of Leads I and II (see Lead III of Fig. 4*B*). Nor is the earlier nomenclature of Einthoven wholly satisfactory, even though it is more consistent in that the deflections are labelled according to their timing in the cardiac cycle and not merely arbitrarily; that is, Q-, R-, and S-waves may be upright or inverted but represent in sequence phases of the first spread of the excitation wave into the ventricles; thus in Lead III of Fig. 4*A* there are in sequence an upright Q-wave, an inverted R-wave, and an upright S-wave.

The timing, however, of the individual deflections is often difficult or

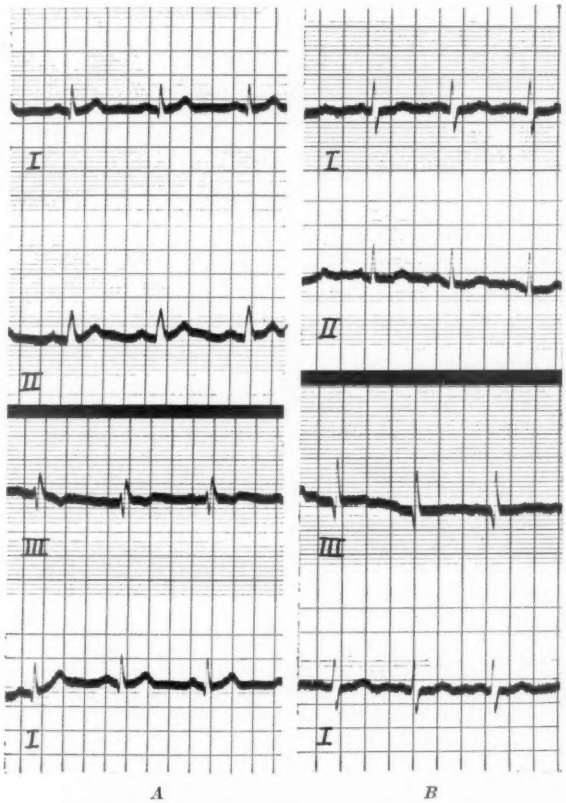


Fig. 4.—Electrocardiograms showing variations of QRS complexes, with Leads I and II taken simultaneously, and Leads III and I taken simultaneously. *A*, The QRS in Lead III presents two upright peaks and one directed downward, the downward deflection corresponding in time with the upright R in Lead I. It represents an inverted QRS complex; *B*, the QRS in Lead III is diphasic, the first deflection being downward and followed by an upward deflection. Timing of the complexes shows that the downward deflections in Lead III occur simultaneously with the upright peaks or R-waves in Lead I.

impossible, when we are dealing with a diphasic or monophasic curve, unless two or more leads are recorded simultaneously. As a matter of fact, the old German designation for the QRS wave, namely I standing for Initialschwankung, is in some respects preferable to QRS. But either designation is suitable if we limit ourselves to a clear, simple description

of what we actually see— thus the QRS wave may be described as consisting of plus and minus deflections extending so many millimeters above or below the baseline without any arbitrary and often misleading attempt to label the individual deflections by exact letter; in Fig. 4*A* the QRS wave in Lead III may be briefly and accurately presented as QRS equals plus 1, minus 2, plus 4, and in Fig. 4*B* QRS_3 equals minus 3, plus 7. For the past five years or more we have used successfully at the Massachusetts General Hospital this method of describing the QRS complexes in electrocardiograms showing low voltage in all leads. The method may usefully be expanded to include all electrocardiograms. Finally, the duration of the individual deflections may be expressed either roughly or accurately by measurement in addition to their direction and amplitude. In the last analysis, however, a reproduction of the complex itself by photograph, tracing, paper, or rough drawing is more instructive than any amount of description, more or less as actual sight of a patient is more valuable than a word picture, no matter how good it is.

SUMMARY

1. Three ventricular complexes have been measured with the Lucas comparator in each of the three leads of 500 human electrocardiograms (150 normal subjects and 350 abnormal subjects) in order to determine the average duration of the QRS waves.

2. The average duration of the QRS complex in 100 normal adults was 0.0777 second. Fifty of the patients were males with an average duration of the QRS time interval of 0.0833 second, and 50 were females with a shorter time interval of 0.0722 second. The average duration of the QRS complex in 50 normal children twelve years of age and under was 0.0719 second with the males having slightly longer duration times. Some particular variation of the ventricular complex such as notching or upright S- or Q-waves accounted for QRS waves wider than 0.0900 second.

3. The only important correlation of the duration of the QRS wave in normal individuals is apparently that with heart size; the taller the person, as a rule, the wider the QRS complex. Neither the age of the patient nor the cardiac rate appeared to have any relationship to the duration of the QRS wave except that the QRS waves of children are in general narrower than are those of adults. The QRS wave was found to be widest most frequently in Lead III.

4. The normal upper limit of duration of the QRS wave of the electrocardiogram in children of twelve years and under may be accepted as 0.09 second, and in adults as 0.10 second. In our series of 50 normal children only 2 showed QRS waves more than 0.09 second long (0.0915 and 0.0992) and in our series of 100 normal adults only 3 showed QRS waves over 0.1 second in duration (0.1006, 0.1017, and 0.1053).

5. In 50 electrocardiograms having an abnormal degree of left axis deviation and an upright T-wave in Lead I the average QRS wave duration was 0.0889 second, and in 50 tracings with an abnormal degree of left axis deviation associated with an inverted T-wave in Lead I the duration time averaged 0.0985 second. The duration time of 0.0870 for the QRS waves in 50 electrocardiograms having an abnormal degree of right axis deviation was thus slightly shorter than that of the cases with an abnormal degree of left axis deviation.

6. The QRS wave durations of 100 electrocardiograms of patients having heart disease without bundle-branch block or an abnormal degree of axis deviation were measured. The average duration of the QRS complex was 0.0779 second in 50 patients having angina pectoris without abnormal T-waves in Lead I or Lead II. The average duration was 0.0827 second for 50 patients who had had coronary thrombosis and showed abnormal T-waves in either Lead I or Lead II.

7. Fifty electrocardiograms interpreted by us as showing intraventricular block of lesser degrees had an average QRS wave duration of 0.1307 second. The average duration of the ventricular complexes was 0.1499 second in the 20 cases of full bundle-branch block with left axis deviation and 0.1412 second in 10 cases of full bundle-branch block with right axis deviation.

8. The average duration of the QRS complexes of 5 ventricular premature beats with left axis deviation was 0.1374 second and of 5 ventricular premature beats with right axis deviation 0.1401 second. The QRS interval averaged 0.0801 second in duration for the normal ventricular responses to premature beats of auricular origin in 5 cases, and 0.1216 second for aberrant ventricular responses to auricular premature beats in 5 other cases.

9. This study has called our attention to the inconsistencies of our present nomenclature of the deflections of the QRS complex. We suggest that a more satisfactory method of describing this complex would be to state positive and negative deflections by appropriate signs with amplitudes expressed in millimeters; thus, QRS equals minus 2, plus 12, minus 5. The duration of the total complex or of the individual deflections may be added if abnormal.

REFERENCES

1. Fahr, G.: An Analysis of the Spread of the Excitation Wave in the Human Ventricle, Arch. Int. Med. **25**: 146, 1920.
2. Ferguson, D., and O'Connell, J. T.: Cardiovascular Observations Including a Series of Electrocardiograms of 1812 Men Without Heart Symptoms, U. S. Naval Med. Bull. **24**: 860, 1926.
3. Holzmann, M., and Scherf, D.: Über Elektrokardiogramme mit verkürtzter Vorhof-Kammer-Distanz und positiven P-Zacken, Ztschr. f. klin. med. **121**: 404, 1932.
4. Jensen, J., Smith, M., and Cartwright, E. D.: The Electrocardiogram in Late Middle Life, AM. HEART J. **7**: 718, 1932.

5. Lewis, T.: Electrocardiographic Plate Studied by Means of the Comparator, Heart 7: 117, 1919.
6. Ibid.: The Spread of the Excitatory Process in the Vertebrate Heart. The Human Ventricle, Phil. Trans. Roy. Soc. 207: 284, 1916.
7. Ibid.: The Mechanism and Graphic Registration of the Heart Beat, London, 1925, ed. 3, pp. 45 and 128, Shaw and Sons, Ltd.
8. Lewis, T., and Gilder, M. D. D.: The Human Electrocardiogram: a Preliminary Investigation of Young Male Adults to Form a Basis for Pathological Study, Phil. Trans. Roy. Soc. 202: 351, 1912.
9. Lincoln, E. M., and Nicolson, G. H. B.: The Hearts of Normal Children. Electrocardiographic Records, Am. J. Dis. Child. 35: 1001, 1928.
10. Seham, M.: Abt's Pediatrics, Philadelphia, and London, IV, 298, 1924, W. B. Saunders Co.
11. Wilson, F. N., and Herrmann, G. R.: Relation of QRS-Interval to Ventricular Weight, Heart 15: 135, 1930.
12. Wolff, L., Parkinson, J., and White, P. D.: Bundle-Branch Block with Short P-R Interval in Healthy Young People Prone to Paroxysmal Tachycardia. Am. Heart J. 5: 685, 1930.

DYNAMIC DILATATION OF THE THORACIC AORTA*

W. K. PURKS, M.D.
BOSTON, MASS.

IN ONE sense of the word all dilatation of the aorta is dynamic dilatation, for without the pressure of the blood within the vessel dilatation would not occur. The term "dynamic dilatation" as commonly used, however, indicates that the internal pressure of the blood is the sole cause of the dilatation and that structurally the aorta is normal and consequently after death returns to normal size. In view of the marked elasticity of the normal aorta which year after year must yield to the impact of the systolic thrust of the heart it seems remarkable that so-called dynamic dilatation does not occur more often. Considered on a purely physical basis, if an individual's diastolic pressure changes from 80 mm. Hg to 120 mm. Hg, his aorta must be distorted to some extent. The distortion may be chiefly manifest as tortuosity or as an increase in width, the tortuosity being due to an increase in length. It is at times important to know whether the dilatation of the thoracic aorta seen by x-ray examination is functional (dynamic) or represents a diseased aorta. Our attention was recently focused on this question by seeing a patient in whom the roentgenologist found an aorta dilated to aneurysmal proportions and in whom the pathologist found an aorta of normal size.

CASE REPORT

E. M. Medical Case No. 42513. A negro chef, aged forty-five years, was admitted to the hospital Feb. 8, 1933, complaining of precordial pain and shortness of breath of three months' duration. His family history was negative. There was no history of syphilis, though he had had gonorrhea twelve years previously. During the last two years he had been troubled by frequent occipital headaches. Three months before admission he first noticed precordial pain. It was persistent though of variable intensity and was accentuated by exertion, at which time it became quite severe. He had frequent paroxysms of nocturnal dyspnea. For two months there had been frequent attacks of temporary blindness in the right eye followed by diplopia.

Physical Examination.—Showed good development and nutrition. He was in moderate respiratory distress. Both optic discs showed a swelling of one diopter. A few white spots were seen in both retinas. There was evidence of vascular disease and one small hemorrhage on the right. The carotid arteries pulsated forcefully. There was no tracheal tug. The lungs showed occasional coarse râles at the right base. The cardiac impulse was 12 cm. to the left of the midline. The left border of cardiac dullness measured 12.5 cm., right border of cardiac dullness 4 cm. from the midline and the supracardiac dullness 6 cm. A systolic murmur was

*From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.

heard at the apex. There was no diastolic murmur. The heart action was regular. The aortic second sound was ringing in character. The blood pressure was 200 mm. systolic and 160 diastolic. The remainder of the examination was not remarkable.

His admission temperature was 99°, pulse 80 and respirations 24. The red blood count was 4,600,000, hemoglobin 82 per cent (S), white blood count 7,500 with a normal differential. The blood Wassermann and Hinton tests were positive. An x-ray picture of the heart showed a widening of the aorta in the anterior, posterior and lateral views.

He had repeated attacks of severe precordial pain, partially relieved by nitroglycerin. On one occasion he had severe pain localized in the epigastrium, associated with a fall of blood pressure to 150/100 and with electrocardiograms quite typical of coronary occlusion. There was no fever, leucocytosis or pericardial friction rub. His blood pressure rose after the attack to 225/135. He continued, however, to have repeated attacks of precordial pain, frequently was covered with sweat, and was extremely weak. Finally on the forty-sixth day in the hospital he had a severe attack and died. Some gastrointestinal symptoms and findings were present but were not pertinent to the present consideration of the case. He was thought to have hypertension, chronic myocarditis and coronary occlusion plus a syphilitic aortitis with aneurysm.

At autopsy surprisingly enough there was neither a dilated aorta nor a coronary occlusion. The aorta measured 7 cm. in circumference just above the valves, and just proximal to the right innominate artery 6.5 cm. in circumference. Its elasticity was extremely well preserved. The proximal aorta was essentially negative, except for a few small atheromatous patches. The heart was greatly enlarged, weighing 520 gm. There were no valve lesions. There were no areas of myocardial fibrosis or softening. There was a generalized mottling with alternating areas of reddish brown and pale brown colors. There was myocardial hypertrophy most marked in the left ventricle. The coronaries were of large caliber, patent throughout and grossly showed little evidence of disease. Other features of the gross pathology need not be described in detail. Suffice it to say, there was a chronic progressive vascular nephritis, acute hemorrhagic colitis, hypoplasia of the thyroid, mesenteric lymphadenitis, pleural adhesions and phleboliths in the prostatic venous plexus. The most significant feature of the microscopic study was the remarkable character of the vascular lesions. Vessels of the various tissues showed essentially the same picture. There was marked degeneration of the intima and media of small aterioles to medium-sized and small arteries. There was in addition to the degeneration an inflammatory cell infiltration and a hyperplastic response. Some vessels showed hyalinization of the media with early evidence of degeneration. These lesions were not diagnostic of a syphilitic peripheral arteritis though suggestive. A detailed consideration of these remarkable lesions is not the province of the present study. Microscopically the aorta showed some thickening of the intima with some degenerative changes. There was a slight bluish stain throughout the media. The structural relations were, however, well maintained. There was no evidence of syphilis. Elastic tissue stains showed an abundance of normal elastic tissue.

This patient did not have a perfectly normal aorta and there was a history of syphilis. He is nevertheless presented as a case of dynamic dilatation because the slight pathological lesions found at autopsy were in an aorta of normal size and yet there was unquestionable dilatation before death. An explanation of the electrocardiographic changes is not essential to the present report. It seems highly probable, however,

that even in the absence of a major focal coronary thrombosis there was such marked disease of the small vessels as to produce a widespread anoxemia of the heart muscle which would alter the electrocardiographic picture.

How can this case be explained and how often does the aorta dilate to abnormal proportions because of pressure changes? The literature contains relatively few references to dynamic dilatation. Some authors feel, as does Wilson,[1] that "It is doubtful if a state of so-called dynamic dilatation ever occurs in a perfectly normal aorta no matter what the blood pressure is." Bayley[2] has recently studied the subject and finds that the conditions in which dynamic dilatation is most often described are aortic insufficiency of rheumatic origin, chronic nephritis with hypertension, hyperthyroidism and cardiac neurosis. He reports three cases in which a dilatation of the thoracic aorta demonstrated by x-ray examination was considered as "dynamic" because organic causes such as syphilis and arteriosclerosis were not present. To the above mentioned conditions in which dynamic dilatation is likely to occur we would add stenosis of the aorta, especially that form of congenital stenosis of the aorta found with coarctation of the aorta.

From the case records of the Peter Bent Brigham Hospital we have studied the x-ray and clinical features of a number of cases in which dynamic dilatation seemed likely to occur. These will be considered in five groups. In considering the whole problem the question at once arises as to just what are the upper limits of measurements for the normal aorta. The limits, of course, vary widely at different ages, and in the last analysis the general impression of the roentgenologist of a given case is probably of more value than are actual measurements compared with a theoretical normal. Our interpretation of whether or not a given aorta is dilated may not conform to the criteria of others, but throughout the study the same criteria have been used and findings in the different groups are comparable. We have considered an aorta dilated when in fluoroscopy it appeared definitely so in the oblique view or when the transverse measurement in the posteroanterior view of the 7-foot plate exceeds 6 cm. Measurements in the oblique view were not often available. In none of these patients was dilatation of the aorta sufficient to produce the murmur of aortic insufficiency; in the group of aortic insufficiency of rheumatic origin there was an aortic insufficiency of organic valve origin.

GROUP I. AORTIC INSUFFICIENCY OF RHEUMATIC ORIGIN

In this group of 39 patients all were under thirty years of age. The average age was 19.1 years. This factor largely eliminates arteriosclerosis as a cause of aortic disease. We may assume that arteriosclero-

sis sufficient to cause gross alteration in aortic contour rarely occurs before the age of forty years. In this group, as in each of the others, all cases in which there was any suggestion of syphilis have been excluded. The average systolic blood pressure, as seen in Table I, was 129.6 mm. Hg, the average diastolic pressure 44.9 mm. Hg, and the average pulse pressure 84.9 mm. Hg. Dilatation of the aorta was recorded in 25.6 per cent, and the aorta was described as tortuous in 2.5 per cent. An effort to compare these figures with those of other observers shows that such studies have not been frequently done. Vaquez and Bordet,[3] in one of the best early books on roentgenography of the heart, state that in aortic insufficiency there is a dilatation of the aorta at its origin from the valvular ring to the level of the arch where it resumes its normal caliber. Wiggers[4] refers to an increase in the aortic shadow in aortic insufficiency. White[5] states that the active oscillations of pressure associated with aortic insufficiency may give rise to very marked pulsation in the aorta with considerable dilatation and prominence of the aorta during systole but with a collapse to *nearly* normal caliber during diastole. Bayley[2] found dilatation of the aorta in 8.4 per cent of his cases. Scott[6] mentions the *frequent* occurrence of dilatation in aortic insufficiency, especially in cases where there is a high systolic pressure and a low diastolic pressure. Holmes,[7] on the other hand, found a normal aortic shadow in all of 15 cases. There is then a rather wide variation of opinion.

In those cases of our series showing dilatation the average systolic blood pressure was 145.2 mm. Hg, the average diastolic pressure 40.6 mm. Hg, and the average pulse pressure 104.6 mm. Hg. That is to say, those with dilatation in contrast to those without dilatation of the aorta had a considerably higher systolic and pulse pressure and about the same diastolic pressure. Clearly then there was much more tension on those that showed dilatation. Were these aortas diseased also? Many observers have described lesions of the aorta as a result of rheumatic fever. These have chiefly been acute processes. Sir Clifford Albutt[8] states that the dilatation which occurs in rheumatic and other forms of aortitis than syphilitic usually subsides as the disease becomes inactive. Our patients were not in the acute phase of the disease. Deutsch[9] has emphasized that aortic disease due to rheumatic fever and other infections is not uncommon. Unfortunately, we do not have autopsy material in the present series and cannot say with certainty that no disease was present in the aorta. Certainly, however, our general experience indicates that in young people coming to necropsy with rheumatic heart disease demonstrable structural disease of the aorta is not often found. Functionally the aorta may be impaired.

GROUP II. HYPERTENSION AND CHRONIC NEPHRITIS WITH HYPERTENSION

In this group there were 21 patients with an average age of 25.5 years. All were under thirty-five years of age. The average systolic pressure was 202.4 mm. Hg, the average diastolic pressure 130.9 mm. Hg, and the average pulse pressure 72.4 mm. Hg. In 42.8 per cent the aorta was dilated, and in 14.6 per cent it was described as tortuous. Here again we find that there are few comparable studies in the literature. Albutt quotes Hart's[10] description of plethoric people whose heart is both enlarged and dilated and whose aorta displays marked distensibility and increased capacity, though it is normal and the increased capacity is not at the expense of loss of resiliency. Sheldon[11] reported marked dilatation of the aorta by x-ray examination in a boy aged ten and a half years who had chronic nephritis and a blood pressure of 210/155 mm. Hg. Post-mortem study showed the aorta entirely normal in size. He regarded the dilatation as a direct mechanical consequence of the increased pressure, the increased pressure being maintained throughout diastole. Evans[12] in a study of arteriosclerosis in children reports one case that had such dilatation of the aorta as to produce pulsation suggesting aneurysm. No x-ray films were taken. The boy, aged fourteen years, had chronic nephritis and a blood pressure of 260/200 mm. Hg. At autopsy the aorta was not dilated. In 14 cases of chronic nephritis and hypertension in adults Smith and Kilgore[13] found x-ray evidence of a dilated aorta in all but 3 cases. They considered the upper limits of normal as 4.5 to 5.5 cm. and classed as dilated all cases with transverse measurements exceeding 6 cm. Contrary to what one might have expected, those patients showing measurements of 7 to 9 cm. were younger than those with measurements of 6 to 7 cm. This quite naturally suggested to them that when hypertension supervenes on an aorta already somewhat stiffened by age, it does not stretch as easily as a younger one would. Autopsies were not done in their series. Holmes[7] states that diffuse dilatation of the aorta is not an unusual finding in hypertension, and White[5] mentions the fact that some of the dilatation seen by the roentgen examination in hypertension is not found at post-mortem since it is temporary and depends upon the intra-aortic hydrodynamic state. Strangely enough although Wilson[1] did not find at autopsy the degree of dilatation evidenced on the x-ray screen in 2 of his cases of hypertension, yet he concluded that dynamic dilatation does not occur.

In regard to the present series the assumption seems justified that the dilatation which was demonstrated was due to the pressure alone because other reasonable causes were not present. We cannot say whether or not the persistent high tension may have exceeded the elastic limit of the aorta and resulted in real dilatation which could have been

demonstrated at autopsy. Even if such had been the case, the aorta probably would have appeared structurally normal under the microscope. Functionally it would not be normal.

GROUP III. HYPERTHYROIDISM

This group is small. It consists of 26 patients, none of whom was over forty years of age. The average age was 29.6 years, the average systolic blood pressure 133 mm. Hg, the average diastolic pressure 64.4 mm. Hg, and the average pulse pressure 68.1 mm. Hg. The average increase in metabolic rate was +58 per cent. Only 4 cases, 15.3 per cent, showed a dilated aorta and none of the aortas was described as tortuous. Bayley[2] found dilatation in 12.1 per cent of 263 cases. His is a more representative series. Analysis of the present group shows that the blood pressure readings were not definitely abnormal; therefore no very high incidence of dilatation of the aorta could be expected.

GROUP IV. CARDIAC NEUROSES

This group consists of 15 patients, with an average age of 28.6 years. All patients over forty years of age were excluded. The blood pressure ranges were quite normal. The average systolic pressure was 120.5 mm. Hg, the average diastolic pressure 71.5 mm. Hg, and the average pulse pressure 49 mm. Hg. Only one case had a dilated aorta. Bayley[2] found dilatation in 9 per cent of 31 cases of cardiac neurosis. We have found only one other reference to the occurrence of a dilated aorta in neuroses. Norris[14] describes paroxysms of dilatation of the abdominal aorta which occur chiefly in neurasthenic women with ptosis. During such attacks there is a marked localized pulsation of the abdominal aorta simulating aneurysm. Attacks are said to begin and end suddenly.

GROUP V. CONGENITAL STENOSIS OF THE AORTA

This group consists of 4 cases of coarctation of the aorta and one of subaortic stenosis. No patient was over forty years of age. The average age was 30.4 years. The average systolic pressure was 168 mm. Hg, the average diastolic 99.6 mm. Hg, and the average pulse pressure 70.8 mm. Hg. Four cases showed widening of the aortic or supracardiac shadow. Vaquez and Bordet[3] believe that the dilatation of the aorta in congenital aortic stenosis is to be explained in the same way as the dilatation of the pulmonary artery in cases of congenital stenosis and that it is due to a functional distention so that it may be perceptible during life but not found after death. They also found dilatation beyond the point of stenosis. Of our 5 cases only one came to autopsy. The patient with subaortic stenosis, aged forty years, had a definitely widened and tortuous aorta by x-ray examination, and yet at post-mortem the aortic arch measured only 6 cm. in circumference and there was no evidence

of dilatation. In the other cases we have no reason to suspect aortic disease and must therefore assume that the dilatation results from increased pressure. Certainly the conditions for producing a functional dilatation are ideal in these cases. That is to say, there is throughout life an increased pressure.

TABLE I

NO PATIENTS OVER FORTY YEARS OF AGE

GROUPS	NO. OF CASES	AVERAGE AGE	SYSTOLIC PRESSURE	DIASTOLIC PRESSURE	PULSE PRESSURE	PER CENT OF CASES DILATED
Aortic insufficiency	39	19.1	129.6	44.9	84.9	25.6
Hypertension	21	25.5	202.4	130.9	72.4	42.8
Cardiac neuroses	15	28.6	120.5	71.5	49.0	6.6
Congenital stenosis of aorta	5	30.4	168.0	99.6	70.8	80.0
Hyperthyroidism	26	29.6	133.0	64.4	68.1	13.5

DISCUSSION

From a review of the literature it becomes apparent that, though isolated cases of dynamic dilatation of the thoracic aorta have been noted and a number of authors have casually mentioned its occurrence, aside from the work of Bayley and of Smith and Kilgore, no one has focused attention upon it as being relatively common. The present study indicates its rather frequent occurrence in aortic insufficiency of rheumatic heart disease, hypertension, and congenital stenosis of the aorta and a slightly less frequent occurrence in hyperthyroidism. In the hypertensive group the elevated pressures in a young individual with an elastic aorta offer the ideal condition for the development of a functional dilatation. In the group of congenital stenosis of the aorta the systolic, diastolic and pulse pressure, though all elevated, are not so high as in the hypertensives. However, the great duration of the process more than offsets the pressure differences, and dilatation is the rule rather than the exception. In the cases of aortic insufficiency and in hyperthyroidism somewhat comparable blood pressures are observed, the chief feature being a high pulse pressure. Though the present study indicates the frequent incidence of dilatation in both groups, it is more common in the aortic insufficiency cases. This is probably due to the younger ages in that group and to the higher pulse pressures. We find no evidence that dynamic dilatation is common in cardiac neuroses. We look upon dynamic dilatation as a purely mechanical process and assume that there are two factors balanced against one another, namely, the elasticity of the aorta and the intra-aortic pressures. Since we do not consider that elastic tissue has any neurogenic control, it could not be influenced by neurogenic factors.

In order to visualize what takes place in dynamic dilatation of the aorta let us assume in a given case a normal aorta in a young individual

with a normal blood pressure. Suppose the pulse pressure is at once increased from 50 mm. Hg to 80 mm. Hg. The aorta, being elastic, yields to the first systolic thrust, but during diastole it will return to its original size unless one of two things occurs. The tension of the initial thrust may exceed the elastic limit of the aorta and the vessel then will not recoil to its normal size. Thereafter it will always be somewhat dilated, and this dilatation will be demonstrable at autopsy. It is doubtful if this ever happens, for Herringham and Wills[15] showed that all aortas when placed in saline for five minutes after they had been stretched with weights up to 200 gm. returned to their original size and therefore are almost perfectly elastic. The other possibility in cases of a high pulse pressure is that although the aorta may be perfectly elastic, its elastic limit having not been exceeded, its rate of recoil may be slow and a second systolic thrust strike it before it has returned to a state of rest after the first. The resulting bombardment of one systolic thrust upon another keeps the aorta dilated, though if the vessel were given a rest it would resume its former caliber which on pathological examination it is found to have. The speed of recoil depends upon the quality of the aorta. This we cannot well evaluate from a pathological study of structure. It is, in general, undoubtedly true that an abundance of elastic tissue represents a highly elastic aorta, but the presence of tissue that takes the stain for elastic tissue does not prove its functional character. It has been shown by various observers that elastic tissue varies widely in functioning power. Though we commonly look upon elastic tissue as an inert substance that responds to distortion according to pure physical principles, it is apparently true that elastic tissue is subject to fatigue. It is easy enough to visualize what happens when an elevation of pressure including the diastolic pressure occurs. Every aorta regardless of its quality, though to varying degrees, must yield when the diastolic pressure rises. The degree of dilatation will depend upon the quality of the elastic substance of the aorta. We do not know what factors alter the quality of elastic tissue. Perhaps it is influenced by heredity, or perhaps it may be altered by acute infections which, however, leave no structural evidence of damage.

In the case report given above we found an aorta which, though it was the site of disease, had not lost its elasticity. It was therefore dilated because it was continuously under a pressure of at least 135 to 150 mm. Hg diastolic and also was subjected to repeated thrusts of a pulse pressure of about 100 mm. Hg.

SUMMARY

1. A review of the literature shows very few references to dynamic dilatation of the aorta, a condition which the present study indicates

is not an uncommon occurrence. It is most common in aortic insufficiency, hypertension, hyperthyroidism, and congenital stenosis of the aorta.

2. A case is reported in which marked dilatation of the aorta demonstrable by x-ray examination was not found at pathological examination.

REFERENCES

1. Wilson, W.: Aortic Dilatation and Aneurysm, Canad. M. J. **12**: 283, 1922.
2. Bayley, Robert H.: Dynamic Dilatation of the Thoracic Aorta, AM. HEART J. **8**: 585, 1933.
3. Vaquez, H., and Bordet, E.: The Heart and Aorta: Studies in Clinical Radiology, New Haven Press, 1920 (Translation by Honej and Macy).
4. Wiggers, C. J.: The Circulation in Health and Disease, Philadelphia, p. 634, 1923, Lea & Febiger.
5. White, P. D.: Heart Disease, New York, p. 182, p. 395, 1931, Macmillan Co.
6. Scott, R. Wesley: Diseases of the Aorta, Oxford System of Medicine, Vol. II, part II, p. 508, Oxford Univ. Press, 1928.
7. Holmes, George: Observations in Aortic Regurgitation, Brit. J. Radiol. **31**: 409, 1926.
8. Albutt, Sir Clifford: Diseases of the Arteries Including Angina Pectoris, New York, 1915, Macmillan Co.
9. Deutsch, G.: Dilatation of Vessels of Non-Syphilitic Origin, Ztschr. f. klin. Med. **90**: 386, 1921; Ab., J. A. M. A. **76**: 1719, 1921.
10. Hart, K.: Zur Frage der Plethora Vera, Deutsch. med. Wchnschr. **38**: 798, 1912.
11. Sheldon, J. H.: Dilatation of the Aorta in Children Associated with Chronic Interstitial Nephritis, Brit. J. Child. Dis. **20**: 216, 1923.
12. Evans, G.: Arteriosclerosis in Children, Quart. J. Med. **16**: 33, 1922.
13. Smith, W. D., and Kilgore, A. R.: Dilatation of the Arch of the Aorta in Chronic Nephritis With Hypertension, Am. J. M. Sc. **149**: 503, 1915.
14. Norris, G. W.: Blood Pressure: Its Clinical Applications, Philadelphia, p. 239, 1914, Lea & Febiger.
15. Herringham, W. P., and Wills, W. A.: On the Elasticity of the Aorta, Being a Contribution to the Study of Arterial Sclerosis, Tr. Roy. Med. Chir. Soc. **87**: 489, 1904.

AN ELECTROCARDIOGRAPHIC STUDY OF VISCEROCARDIAC REFLEXES DURING MAJOR OPERATIONS*

C. C. MAHER, M.D., P. J. CRITTENDEN, PH.D., AND P. F. SHAPIRO, M.D.
CHICAGO, ILL.

THE subject of viscerocardiac reflexes during and after major operations has been investigated by others, and a review of their work is given by Owen.[1] The data herein reported are a continuance of the work of Owen,[1] and of Crittenden and Ivy.[2]

PROCEDURE

The electrodes used in making these electrocardiographic observations were skin suture needles about four inches long. They were placed subcutaneously in the second or third, and fifth and sixth intercostal spaces on the left side near the midline. This ruled out many of the somatic tremors which are marked with the ordinary skin contact electrode. Ressinger[3] used this type of electrode in his investigation.

The control electrocardiogram was usually taken the night before the operation. When the operating schedule offered an emergency case or one of special interest, the control was taken from one-half to one hour prior to the anesthesia.

Electrocardiograms were made at various intervals during anesthesia and the operative procedures, and also from four to six hours postoperatively. Additional electrocardiograms were usually made the next day and also one week later.

The progress of the operations was observed by one of us who signalled the operator of the electrocardiograph when to take an electrocardiogram. The surgeons cooperated in synchronizing manipulations likely to give viscerocardiac reflexes with the taking of the electrocardiograms.

TYPES OF CASES

Eighty-nine cases were studied. The type of cases varied. They included: cholecystectomy, 16 patients; appendectomy, 9; gastric resection, 7; cholecystectomy and appendectomy, 4; herniotomy, 5; hemorrhoidectomy, 4; uterine fibromyomectomy, 3; hysterectomy, 4; hydrocele, 3; colostomy, 3; thyroidectomy, 3; salpingectomy, 2; exploratory laparotomy, 2; cholecystotomy, 3; perineorrhaphy, 1; enteroanastomosis, 1; nephrectomy, 1; thoracoplasty, 1; vaginal fistula, 1; salpingectomy and appendectomy, 1; cesarean section, 1; cyst of the broad ligament, 1; ovarian carcinoma, 1; ovarian cyst, 1; uterine suspension, 1; vaginal plastic, 1; tuberculous peritonitis, 1; generalized carcinomatosis, 1; lumbar sympathectomy, 1; ulnar neurolysis, 1; radial neurolysis, 1; incision of cellulitis, 1; normal deliveries, 3.

In the early part of the work a general survey was made of as many different types of operations as could be utilized. Later it seemed that viscerocardiac reflexes might be obtained best from the upper abdominal operations. Special effort was made to find cases with such complications as jaundice, pancreatitis or previous cardiac disease. Previous work demonstrated that these conditions were

*From the Departments of Physiology, Medicine and Surgery of the Northwestern University Medical School and the Department of Surgery of the Cook County Hospital, Chicago. This work has been aided by a grant from the Josiah Macy, Jr., Foundation.

likely to sensitize the viscerocardiac reflex mechanism. The cases studied included fifty-four women and thirty-five men. Their ages varied from twelve to seventy-three years.

ANESTHESIA

Various types of anesthetics were used: ether, 58 patients; ether with nitrous oxide induction, 12; nitrous oxide only, 6; nitrous oxide and local anesthesia, 2; local anesthesia, 3; spinal anesthesia, 3; peridural anesthesia, 1; avertin, 1. Two of the deliveries were conducted without anesthesia.

RESULTS

P-Wave.—The most outstanding electrocardiographic observation made during the entire series was the P-wave change which occurred with the patient under deep ether anesthesia. The P-waves would disappear with the assumption of nodal rhythm and evidence of retrograde conduction in the auricles. This occurred in twenty-eight of the fifty-eight straight ether cases, and in four of the twelve nitrous oxide ether cases. In the latter, nodal rhythm appeared only after the patient was under deep ether anesthesia. With two exceptions, it never appeared in the cases using nitrous oxide only, nor in the avertin, spinal, peridural or local anesthesia cases. These exceptions occurred in one case under spinal and in one under nitrous oxide novocain anesthesia.

Besides these nodal rhythm cases, seven patients showed a shortening of the P-R interval without actually going over into nodal rhythm. In four of these cases there was a decrease of from 0.03 to 0.04 second when the patient was brought under deep ether anesthesia. In two cases the P-R abbreviation occurred later in the operative procedure. In one case a decrease of 0.03 second was specifically noted with dilatation of the rectum, but at this point also the anesthesia was deepened by the patient's increased respirations.

Other changes noted in the P-waves were that they became depressed during deep ether anesthesia without going into nodal rhythm (two cases). They became diphasic in two cases under deep ether anesthesia. In one case they became larger in the second stage of anesthesia, only to disappear in the third. In one thyrotoxic case, the T- and P-waves were practically fused. This fusion became more marked as the tachycardia increased during the anesthesia, and was probably only a result of the increased heart rate. The P-wave was negative in one case for two hours after the operation, and then positive. In one case it was present, but decreased in size for six hours after operation, and then returned to normal size. In one case the P-R interval was increased by 0.06 second during the operation. In one case an increase of 0.04 second was noted one week after operation.

Voltage.—Certain voltage changes were found. They appeared in the excitement stage of anesthetic induction, or when the patient was

straining on the operation table, and sometimes during operative procedures. An increase in voltage was seen in one case when the pylorus was crushed and the stomach pulled down for resection. It was seen once when the gall bladder was being pulled up, once during palpation of a carcinomatous stomach. A decrease in voltage was also seen once when the appendix was being ligated, and once when the rectum was being dilated. The reaction was absent many times, however, when the surgeon, with specific force, pulled on the stomach, gall bladder, appendix, thyroid, hernial sac, uterus, hemorrhoid or adhesions, or explored the abdomen.

QRS Complexes.—QRS changes occurred in fifteen patients having ether, or ether with nitrous oxide induction, and in one patient under avertin. In one patient who was slightly jaundiced the R-wave was decreased 2 mm. during anesthesia and operative procedure but was increased 2 to 4 mm. postoperatively. In one case the S-wave deepened during the excitatory phase of the anesthesia. Dilation of the rectum caused a diphasic complex in another. In one case there was a mild but definite slurring of the QRS toward the end of the operation. In another, the QRS became widened and notched while the gall bladder bed was being packed. In one case (thoracoplasty under avertin) the QRS became widened and slurred after the patient "went bad" on the table. A week postoperatively in one hydrocele case, the wave was slurred and notched, indicating a myocardial disturbance. Postoperatively in one case the QRS complex was depressed the day after operation; in another case it increased one week later.

T-Wave.—Anesthetic induction depressed the T-waves in seven cases; in four of these they remained depressed throughout the entire operative procedure. In one case the T-waves showed some inversion during deep nitrous oxide anesthesia. They stayed flat through the ether administration and operation, but became upright again when the peritoneum was being closed. During anesthetic induction the waves increased in two other cases, disappeared in two and became more pointed in one.

The waves vanished in four cases only late in the operative procedure. They were seen to disappear with palpation of a carcinomatous mass, manipulation of the duodenum, pulling on a hernial sac, placing an appendiceal purse string, etc., but the association was neither constant nor specific. Occasionally they became inverted and sometimes diphasic. Postoperatively the wave became markedly decreased in two cases, absent in one, and negative in two.

Rates.—The changes in rates were taken as differences from the immediately preceding rate rather than from that of the control. In one thyrotoxic case, the control rate was 190 resembling an auricular flutter with 1:1 ratio. The rates were usually increased with anesthetic

induction, fluctuated irregularly with various operative maneuvers, and became normal soon after the completion of the operation.

Thirty-one cases showed an increase of from twenty to eighty beats per minute with anesthetic induction. Four showed a decrease of from fifteen to twenty-five during early anesthesia. In two cases under nitrous oxide, the rate was increased twenty and forty-five, to be decreased later by ether, sixty and forty-five respectively. One case showed a gradual increase of thirty-five during anesthesia and operative procedure. In one case there was a consistent tachycardia throughout. The following changes occurred at various intervals during operative procedure. Pulling on the gall bladder decreased the rate forty-five beats per minute in two cases and twenty-five in another. Cutting the skin was associated with an increase of forty in one case and cutting the peritoneum with an increase of fifty in another; the latter procedure caused a decrease of thirty and fifty-five in two other cases. In an appendectomy, traction on the mesentery of the appendix caused a decrease of seventy-five. In a herniotomy, traction on the sac caused an increase of thirty-five.

Extrasystoles.—Auricular extrasystoles occurred in five cases, ventricular extrasystoles in four cases and nodal extrasystoles in two. In two other cases there were both auricular and ventricular extrasystoles. The auricular extrasystoles began in one cholecystotomy case while the skin incision was being made and disappeared when the gall stone was removed. They appeared again when the peritoneum was being closed. They appeared also during incision of a hernial sac, pulling on an omentum, during clamping of hemorrhoids and packing a gall bladder bed. They were also seen, however, without operative stimuli, e.g., during the excitatory stage of anesthesia, and again one day postoperatively.

The ventricular extrasystoles appeared during palpation of a carcinomatous mass, during clamping of hemorrhoids, closing of the peritoneum, pulling on a hernial sac, and packing of a gall bladder bed. They were also seen, however, during anesthetic induction. In two cases, extrasystoles of ventricular origin were present in the controls, during anesthesia induction and postoperatively, but were absent during the operative procedure.

In a thyroidectomy under nitrous oxide, one nodal extrasystole appeared during early anesthesia. In a cholecystectomy under ether, interpolated beats of nodal origin appeared when the cystic duct was being cut.

ABNORMAL BEATS

All these electrocardiographic abnormalities were of such different character and occurred at such various intervals that a brief protocol on each patient seems desirable.

CASE 1.—Appendectomy-cholecystectomy. Ether. The patient was slightly jaundiced at the time of the operation. The R voltage was lowered about 2 mm. during anesthesia and operative procedure, increasing 2 to 4 mm. postoperatively. During the operative procedure the T-wave was depressed and a sinus arrhythmia was noted.

CASE 6.—Cholecystectomy. Ether. During the operative procedure the QRS had a phasic variation and the T-wave was flattened. The skin incision caused a new auricular complex which persisted until the removal of the gall stone. A similar change was noted when the peritoneum was sutured.

CASE 8.—Colostomy. Carcinoma of the rectum. Ether. The sino-auricular node was depressed throughout the operative procedure. The T-wave was depressed during anesthesia induction and the operative procedure.

CASE 10.—Appendectomy. Ether. The T-wave was depressed throughout the operative procedure and slowly returned to normal postoperatively. It was again depressed on the fifth day and was absent two weeks later. Cutting the peritoneum caused a depression of the sino-auricular node which was still depressed five days later.

CASE 13.—Cholecystotomy. Ether. The R voltage was markedly decreased the first day postoperatively, and the T-wave was depressed during the operative procedure. The sino-auricular node was markedly depressed during anesthesia. There was a mass in the region of the duodenum, the palpation of which caused an extrasystole of ventricular origin.

CASE 16.—Herniotomy. Ether. The T-wave disappeared with tension on the hernial sac, and there were also extrasystoles of auricular origin during the incision of the hernial sac. Nodal rhythm was present during the "painting" of the skin.

CASE 18.—Hemorrhoidectomy. Light nitrous oxide. The T-wave became negative during the operative procedure and also persisted postoperatively. Extrasystoles of auricular and ventricular origin were noted with clamping of the hemorrhoids. Dilating the rectal sphincter caused marked somatic tremors.

CASE 19.—Benign rectal tumor. Ether. The T-wave became absent during the operative procedure and negative postoperatively. The skin incision caused a complete auriculoventricular disassociation. When the fascia was reached sinus rhythm had returned.

CASE 22.—Hysterectomy. Ether. There was a slight variation in the QRS voltage with the operative procedure. Ventricular extrasystoles, three in sequence, followed by a nodal beat, occurred with the sewing of the peritoneum.

CASE 27.—Fibromyomatous uterus. Ether with nitrous oxide induction. Early anesthesia decreased the P-R interval 0.04 second, and there was also a sino-auricular block which disappeared in later anesthesia.

CASE 28.—Uterine suspension. Ether. The QRS complex was depressed after anesthesia, and the T-wave was depressed during the operative procedure and postoperatively. There was retrograde conduction and nodal rhythm with pulling on the round ligament and tube, showing simultaneous auricular and ventricular conduction. This lasted for several minutes when sinus rhythm again appeared.

CASE 29.—Strangulated hernia. Ether with nitrous oxide induction. There were extrasystoles of ventricular origin with pulling on the hernial sac and strangulated omentum. The auricular complex changed in character for three successive beats

after each extrasystole. Extrasystoles occurred at various times during the operative procedure. These changes were not noted with the control anesthetic induction or postoperatively.

CASE 31.—Appendectomy. Cholecystectomy. Ether. The QRS was notched in the control, but this was more apparent after the anesthesia was administered. There was nodal rhythm early in the operative procedure with a rate of 60. Clamping the appendix caused a return to sinus rhythm.

CASE 34.—Inoperable gastric carcinoma. Ether. The T-wave became flattened with anesthesia and remained so throughout the operative procedure. There was a change from sino-auricular to nodal rhythm.

CASE 36.—Hemorrhoids. Nitrous oxide with some ether. The P-wave became negative with clamping of the hemorrhoids and with packing. There were extrasystoles of auricular origin with dilation of the sphincter and clamping of the hemorrhoids. Ventricular escape occurred during the exploration of the rectum.

CASE 37.—Cholecystectomy and appendectomy. Ether. The T-wave was flattened postoperatively and became inverted six hours after the operation. During early anesthesia there was ventricular escape with a return to sinus rhythm which occurred twice in a short period of time.

CASE 39.—Cholecystectomy. Ether. Ventricular escape and nodal rhythm was observed when the gall bladder was under tension, and with clamping of the cystic duct.

CASE 42.—Cholecystectomy. Ether. In some instances during the operative procedure there was a retrograde conduction with nodal rhythm.

CASE 43.—Cholecystectomy. Ether. The T-wave showed some slight variation in voltage during the operative procedure. There was a complete block or ventricular escape while the peritoneum was being cut.

CASE 44.—Hydrocele. Ether. QRS complex was notched and slurred one week later showing myocardial disturbance.

CASE 45.—Gastric carcinoma. Ether. The T-wave disappeared with manipulation of the duodenum. There were extrasystoles of auricular origin with excitement during anesthetic induction, clamping of the blood vessels, and cutting of the fascia. There were also extrasystoles of ventricular origin during the first two procedures noted above.

CASE 47.—Cholecystectomy. Appendectomy. Ether. The P-wave became smaller during the operative procedure. The P-R interval lengthened 0.04-0.06 second during the operative procedure. The S voltage likewise increased. The first day, postoperatively, there was an extrasystole of auricular origin.

CASE 48.—Appendectomy. Procaine and nitrous oxide later, just after completion of incision and before locating the appendix. In early nitrous oxide anesthesia, the T-wave was absent. Ligation of the appendix caused it to become small, and while the purse string was being placed, it became negative or diphasic. It was negative with cutting the appendix and persisted postoperatively one week later. The placing of the purse string caused ventricular escape, and nodal rhythm supervened. Cutting the appendix changed the auricular complex. The P-wave became small in size and disappeared, with inversion for four beats, and then returned to normal.

CASE 49.—Fibromyomatous uterus. Ether. In early anesthesia the T-wave was inverted and diphasic with manipulation of the uterus. In exploration of the lower abdomen there was ventricular escape with supervention of nodal rhythm, and retrograde conduction was readily demonstrated.

CASE 57.—Appendectomy. Ether. A case of rheumatic heart disease. A mild waviness of the base line was suggestive of fibrillation of the auricle. The P-waves disappeared under ether.

CASE 58.—Thyroidectomy. Nitrous oxide. The control showed a very rapid rate of 190, which resembled an auricular flutter with a 1:1 ratio. There was one nodal extrasystole during early anesthesia.

CASE 59.—Cecostomy. Ether. During the early operative procedure the T-waves became more prominent. Later they were diphasic, and by the end of the operative procedure there occurred a definite but mild slurring of the QRS.

CASE 60.—Exploratory laparotomy. Nitrous oxide and ether. P-waves disappeared during deep ether. They returned later. Some flattening of the T-wave was noted during the latter part of the operation.

CASE 62.—Salpingectomy. Ether. During the course of the operation, P-waves became lower and T-waves slightly higher.

CASE 70.—Appendectomy. Nitrous oxide and ether. During deep nitrous oxide anesthesia, the T-waves showed some inversion and remained flattened through the ether anesthesia. They became upright, however, while the peritoneum was being closed, and the ether was still being given.

CASE 71.—Hysterectomy. Ether. Under deep anesthesia, the P-wave disappeared. It reappeared momentarily while the patient was changed to the Trendelenburg position. It disappeared when the ether was deepened for skin incision. It reappeared for a minute during the last stages of the operation only to disappear again until the ether was lightened.

CASE 72.—Hysterectomy. Ether. Nodal rhythm appeared for a brief interval toward the end of the operative procedure.

CASE 77.—Gastric resection. Ether. The rate slowed to 80, and the voltage increased after the pylorus was crushed and the stomach pulled out for resection.

CASE 79.—Perineorrhaphy. Ether. Nodal rhythm appeared as soon as the patient was under deep ether anesthesia.

CASE 82.—Cholecystectomy. Nitrous oxide and ether. On packing the gall bladder bed, QRS widened and became notched. The height of T-wave increased and the auricular complex disappeared. Ventricular rhythm was disturbed by probable extrasystoles.

CASE 83.—Cholecystectomy. Ether. Nodal rhythm began as soon as the patient was under deep ether anesthesia. It was associated with a mild increase in voltage.

CASE 85.—Thyroidectomy. Nitrous oxide. T-waves and P-waves were practically fused in the controls. This fusing became more marked as the rate increased during the anesthesia. Marked tachycardia (140) developed as the incision was being closed.

CASE 87.—Thoracoplasty. Avertin. The patient "went bad" on the table. At this point the QRS widened and slurred, and a marked tachycardia developed.

CASE 89.—Cholecystectomy. Ether. The P-wave was enlarged under moderate ether anesthesia but disappeared under deep ether anesthesia. It reappeared during

the early operative procedures, but disappeared when the ether was deepened in the later stages of the operation. At this point also, namely when the cystic duct was being cut, interpolated beats of nodal origin appeared.

CASE 90.—Cholecystectomy. Ether. Under deep ether anesthesia the P-waves became diphasic. In several of the electrocardiograms there were numerous small diphasic complexes which were probably artefacts but might have represented auricular activity.

CASE 91.—Cholecystectomy. Ether. Patient jaundiced. The only change noted was the appearance of nodal rhythm.

CASE 92.—Cholecystectomy. Ether. Nodal rhythm under deep ether anesthesia.

CASE 93.—Cholecystotomy for acute pancreatitis. Ether. Nodal rhythm under deep ether anesthesia.

CASE 94.—Cholecystectomy. Ether. Patient jaundiced. Low voltage while the patient was straining. Nodal rhythm began when the patient was fully under. P-waves returned for a short time during the course of probing the common bile duct but disappeared again while the same procedure was still under way. P-waves reappeared only when the ether was stopped.

Disappearance of Control Abnormal Beats.—There was also another group of patients in whom abnormal beats were present in the control electrocardiogram, but were conspicuously absent later.

CASE 20.—Cesarian section. Ether. The control showed a sinus arrhythmia which disappeared with the operative procedure.

CASE 24.—Neurolysis of the ulnar nerve. Ether. The control waves showed extrasystoles of ventricular origin which were present with administration of the anesthetic but disappeared during the operative procedure and reappeared postoperatively.

CASE 32.—Tuberculous peritonitis. Ether with nitrous oxide induction. The control showed extrasystoles of ventricular origin which disappeared during the operative procedure and reappeared postoperatively.

Somatic Tremors.—Three other cases showed marked somatic tremors with certain operative procedures.

CASE 4.—Vaginal fistula. Ether. There were marked somatic tremors with dilation of the rectum.

CASE 9.—Hydrocele. Ether. There were tremors with puncturing of the hydrocele.

CASE 18.—Hemorrhoidectomy. Light nitrous oxide. There were marked somatic tremors with dilation of the rectum.

Obstetrical Cases.—Three obstetrical cases were followed during delivery from the first to the third stages. No marked changes were noted except in the following cases. During pain in the first stage there was an increase of 70 in the heart rate. In the latter part of the first stage, the rate slowed. Very marked somatic tremors were noted in all three cases.

DISCUSSION

The most frequent important cardiac change found in these observations was disappearance of the P-wave with assumption of nodal rhythm. Deep anesthesia was probably the single most important factor in eliciting it. The P-wave change was seen practically only in these cases in which deep anesthesia was used. Thus it was seen in thirty-two of the seventy cases in which ether was used, and only twice in the nineteen cases in which some lighter anesthetic was given. Among the ether cases it was seen especially in those cases requiring deeper anesthesia. Thus it appeared in fourteen of the twenty gall bladder cases, and in four of the five herniotomies, and in none of the three hydroceles. P-wave changes never appeared before the patient was under moderate or deep anesthesia. They usually appeared some time during the third stage of anesthetic induction and before any operative manipulation had begun. They usually disappeared near the close of the operation when the anesthetic was discontinued.

Occasionally nodal rhythm did not appear until late in the operative procedure. In these cases the patients were not deeply anesthetized until some particular manipulation late in the operative procedure required it. Such manipulations varied greatly in type, including pulling on the round ligaments, dilation of the rectum, ligating the cystic duct, etc. The anesthesia was always deepened at these points, but it is impossible to state in these instances whether the deepening of anesthesia or the operative manipulation was responsible for the nodal rhythm.

In four cases nodal rhythm appeared, then disappeared and reappeared several times during the operation. It was observed that its appearance and disappearance corresponded to those periods in which the anesthesia was increased and decreased, respectively. It was also noted that during the course of a single procedure, e.g., probing the common bile duct, the P-wave would at first appear normal. Then the P-R interval would gradually shorten and the P-wave become depressed or notched until it was lost in the ventricular complexes. It might then appear superimposed on some limb of the QRS or on the R-T segment. It would seem here that the operative manipulation had induced the nodal rhythm, but within a minute or less while the same procedure was under way, the process might reverse, and normal sinus rhythm be reestablished.

Deep anesthesia, however, is not the only factor in the production of these changes. Thirty-eight of the seventy ether cases failed to show the P-wave changes. Even with the same operation and same depth of anesthesia, they sometimes appeared and sometimes did not. There were probably several uncontrollable factors which influenced susceptibility to these changes. These clinical observations, however,

did not establish what those factors were. Age and sex were not important. The patients varied from twelve to seventy-three years in age. Cardiac changes were as frequent in the older patients as in the younger. They were as common in women as in men. Moreover, the condition of the patient had little to do with these changes. We selected certain toxic and septic patients, one very anemic patient, one emaciated patient and one in profound shock. The cardiac changes produced at operation were no different in character and frequency from those seen in patients in good condition. Apparently the general condition of the patient is not related to his susceptibility to cardiac changes. Thyrotoxicosis also failed to play any rôle except in giving a basal tachycardia. We had two cases in which there was previous cardiac disease, one rheumatic heart disease, the other coronary sclerosis, and these two also failed to show any noteworthy cardiac changes.

In a previous paper,[2] evidence obtained from dogs suggested that icterus sensitized the vagal mechanism, and thus might account for the greater incidence of cardiac irregularities obtained in icteric animals on distention of the biliary passages. Three of our gall bladder patients were jaundiced. The changes produced in them, however, were no different in character and frequency from those produced in the nonjaundiced gall bladder patients. Though none of these factors could be established singly as of direct importance, it may be that some summation of them is what finally determines an individual's susceptibility to cardiac changes.

The type of anesthesia was not important except as it controlled the depth of anesthesia. In a recent article by Hill[4] it is stated that chloroform was more toxic to the heart than other anesthetics. The most outstanding irregularity he found was the production of multiple extrasystoles of ventricular origin. They occurred primarily during anesthetic induction, disappeared with deep anesthesia, and were not related to the operative procedure. Such changes were not observed in this series. However, chloroform was not used in any of our cases. Ether was used in almost all cases in which cardiac changes were produced. The three exceptions, one case under spinocain, one under avertin, and one under nitrous oxide and novocain, demonstrate, however, that it is not the ether which is specifically responsible for these changes, but rather the depth of anesthesia.

Minor changes in the P-wave and shortening of the P-R interval are interpreted in the same light as the development of nodal rhythm. The voltage changes were probably a general somatic reaction rather than a specific viscerocardiac reflex. Their association with any operative manipulation was neither constant nor specific, and they appeared also during anesthesia before any operative procedure was started, and even after operation and anesthesia had been stopped.

The same may be said of the T-wave changes. QRS changes indicate myocardial disturbance. They too appeared to be related to the toxicity of deep anesthesia rather than to any particular operative stimulus. Only twice in fifteen times in which it was observed did it seem that the QRS change was closely associated with an operative manipulation. In one case it was the packing of a gall bladder bed; in the other it was the evacuation of an empyema which apparently produced the change.*

Extrasystoles and slowing of rate appeared as sharper responses. They were seen several times directly associated with some operative visceral stimulation, and it seemed that here on occasion a true viscerocardiac reflex had been produced. Extrasystoles appeared in thirteen of the eighty-nine cases. In two cases they appeared during anesthetic induction, and in one case postoperatively. Slowing of the pulse appeared in eleven of the eighty-nine cases. It appeared in six cases during anesthetic induction. In ten cases extrasystoles appeared in immediate association with a definite operative maneuver, such as pulling on a gall bladder (two cases), palpating a carcinomatous mass, crushing a hemorrhoid, incising a hernial sac (two cases), pulling on the omentum, etc. In four cases the pulse slowed while the gall bladder was being pulled, in two cases while the peritoneum was being cut, and once during traction on the mesentery.

The type of operation did not seem to be important. An especially large number of gall bladder patients (twenty cases) were studied because previous work[2] indicated that viscerocardiac reflexes might best be obtained from the biliary tract. Only four of the twenty showed extrasystoles. The type of operative manipulation did not seem to be important because extrasystoles appeared after all types of unrelated stimuli. Only two of the gall bladder cases showed extrasystoles in definite association with manipulation of the biliary tract. Four bradycardial responses were directly related to pulling on the gall bladder, yet they were also seen after other manipulations. From the proximity of the stomach to the celiac plexus and diaphragm it seemed that gastric operations might be likely to elicit viscerocardiac reflexes. Ressinger[3] found marked changes with a case of carcinoma of the cardia. We, too, found electrocardiographic changes in four cases of operation for gastric neoplasm, but three other cases were negative. In the four positive cases, only once was a bradycardia related to direct manipulation of the stomach. Extrasystoles were not seen in any of the gastric cases. In these observations there was no constant, specific connection between type of operation or type of operative stimulus and electrocardiographic disturbance. Only the

*Bettman and Priest showed that if thoracoplasty caused a simple lateral shift of the heart, no electrocardiogram changes were produced. If, however, it caused rotation of the heart on its A-P axis (so that flow through the great vessels at the base was compromised), changes were produced.

bradycardia on pulling the gall bladder was suggestive of such a connection. Even in positive cases when the surgeon was asked several minutes later at the same operation, or at some other similar operation, to repeat the particular manipulation with special force intended to elicit the cardiac disturbance, almost always nothing happened. The failure to repeat the result at the same operation might be explained as a fatigue inhibition. The failure to repeat it at a subsequent operation might be explained on the basis of some uncontrollable variable.

The difficulty of obtaining electrocardiographic changes in response to visceral stimulation and particularly the difficulty of establishing any constant or specific connection between them does not, however, refute the importance of neurological connection between the viscera and the cardiac rhythm reflexes. The fact remains that in a certain, albeit small, percentage of cases electrocardiographic changes were produced which were directly related, in time at least, with a definite operative stimulus. The association of such changes with visceral stimuli has been demonstrated previously by experimental studies on animals[2] and by observations on normal unanesthetized human subjects. The routine conditions of clinical surgical procedures introduced several factors, however, which could not arbitrarily be eliminated, and which inhibited the cardiac responses. The positive results which were obtained were probably due to the fact that in exceptional instances there was sufficient gap in the inhibitions to admit a viscerocardiac response.

The deep anesthesia itself, though apparently responsible for the P-wave changes and perhaps partly responsible for the T-wave and QRS changes, may have been the most important factor in preventing the appearance of extrasystoles, bradycardias and other gross changes. The preoperative morphine and atropine which all our patients routinely received may have had similar inhibitory effects. Thus it has been found that in experimental animals the injection of apomorphine, by causing nausea and vomiting, will elicit cardiac irregularities in a certain proportion of cases. Deep anesthesia, however, or large doses of morphine will abolish this effect (Crittenden). The pathway for the cardiac response is largely vagal; and atropine alone, it has been found, will also abolish the viscerocardiac reflexes produced by experimental apomorphine visceral excitation. In three of our own cases there was an abnormal cardiac rhythm during the controls, during anesthetic induction and postoperatively. During the operative procedure, however, with the patients under deep anesthesia, and morphine and atropine the cardiac abnormalities vanished. These three cases demonstrated quite definitely that deep anesthesia and morphine and atropine could abolish cardiac irregularities. It is conceivable that they exerted a similar inhibitory effect on the rest of our cases,

and thus could have succeeded in preventing the production of these irregularities. *From a clinical standpoint, it may well be considered a favorable circumstance that the routine conditions of major surgical procedures automatically suppress the development of cardiac changes under visceral stimulation.*

CONCLUSIONS

During major surgical procedures the most frequent electrocardiographic change is suppression of the P-wave and assumption of nodal rhythm. This occurred in thirty-four of the eighty-nine cases, and was probably chiefly a function of deep anesthesia.

The type of anesthetic, the age and general condition of the patient, the cardiac condition of the patient, the type of operation or of operative procedure or the underlying pathology for which it was done did not seem to be important in producing this change.

Extrasystoles appeared in ten cases and bradycardia appeared in seven cases in apparent direct association with a visceral stimulation. No constant or specific relation could be established, however, between the surgical procedure and the cardiac response.

REFERENCES

1. Owen, S. E.: A Study of Viscerocardiac Reflexes, AM. HEART J. **8**: 496, 1933.
2. Crittenden, P. J., and Ivy, A. C.: A Study of Viscerocardiac Reflexes, AM. HEART J. **8**: 507, 1933.
3. Ressinger, H.: Electrocardiographic Investigation During Surgical Procedure, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **40**: 504, 1927.
4. Hill, I. G. W.: The Human Heart in Anesthesia, Edinburgh, M. J. N. S. **39**: 533, 1932.
5. Lenox, W. G.: Graves, R. C., and Levine, S. A.: An Electrocardiographic Study of Fifty Patients During Operation, Arch. Int. Med. **30**: 57, 1922.
6. Marvin, H. M., and Pastor, R. B.: The Electrocardiogram and Blood Pressure During Surgical Operation and Convalescence, Arch. Int. Med. **35**: 768, 1925.
7. Buchbinder, W. C.: The Electrocardiogram in Experimental Obstructive Jaundice, Proc. Soc. Exper. Biol. & Med. **27**: 371, 1930.
8. Buchbinder, W. C.: Experimental Obstructive Jaundice, Arch. Int. Med. **42**: 743, 1928.
9. Bettman, R., and Priest, W.: Electrocardiographic Studies Before and After Chest Operations, AM. HEART J. **5**: 366, 1930.

Department of Clinical Reports

OBSERVED ONSET OF BUNDLE-BRANCH BLOCK WITH CORONARY THROMBOSIS 45 HOURS LATER*

C. Bruce Perry, M.D.
Bristol, England

THE following case appears worthy of record because of the fact that the development of a bundle-branch block was observed electrocardiographically without any symptoms or change in physical signs.

A. P., aged fifty-nine years, railway-shunter. November 17, 1933, referred to hospital by Dr. A. N. P. Milner, his panel doctor, for further investigation.

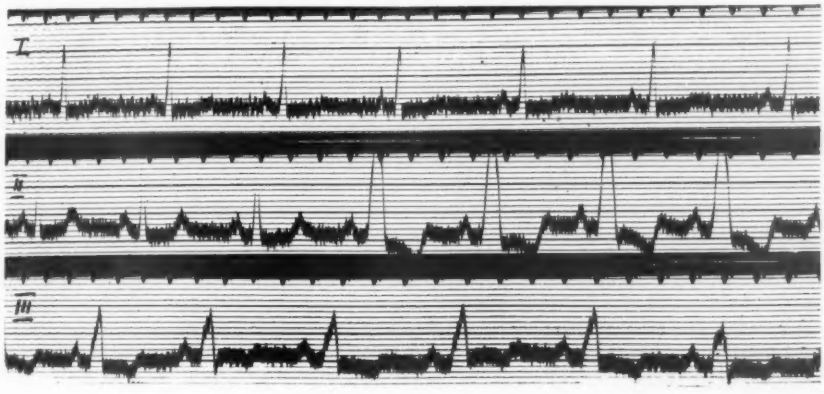


Fig.1.—Electrocardiogram showing the onset of bundle-branch block in Lead II. Time marker indicates fifths of seconds.

Patient complained of attacks of "heaving" pain in the middle of the chest. This pain was caused by walking, particularly up a hill, and passed off in one or two minutes when he stopped. He had noticed some dyspnea on exertion during the past year, but the first severe attack of pain was six weeks ago. The pain was usually associated with dyspnea.

No previous illnesses of importance.

Family History.—Father died of a "seizure" aged sixty years. Mother died aged sixty-five years from "old age." One brother died of "cancer" aged sixty years. Other siblings alive and well.

Examination.—Radial and brachial arteries definitely thickened. No venous congestion in the neck. Apex beat and cardiac dullness normal, heart sounds faint except the second sound at the aortic area which was accentuated. Blood pressure

*From University Center of Cardiac Research, General Hospital, Bristol, England.

190/100 mm. Retinal arteries appeared arteriosclerotic and the veins were full. There were no abnormal physical signs in the lungs, abdomen or nervous system. The urine contained no albumin or sugar. Wassermann reaction was negative. An x-ray film showed no appreciable cardiac enlargement. An electrocardiogram (Fig. 1) showed a normal tracing in Lead I and in the first half of Lead II, after which the ventricular complexes suddenly assumed the features of a bundle-branch block. Another electrocardiogram taken one and one-half hours later (Fig. 2) showed a bundle-branch block of "indeterminate" type in all three leads. There were no symptoms associated with this change in the character of the electrocardiogram and no alteration in the clinical physical signs. The patient stated that he felt quite well and was unwilling to remain in hospital.

Subsequent history.—He returned home and was apparently well until November 19, when he was seized with a severe substernal pain at 9 A.M. following an attack of flatus. The skin was cold and clammy and he complained of faintness. The pain lasted until 2 P.M. On this day the patient was visited by Dr. A. N. P. Milner, to whom I am indebted for this history. November 22, no further pain but complaints of great weakness. Suddenly his speech became very difficult and slurred,

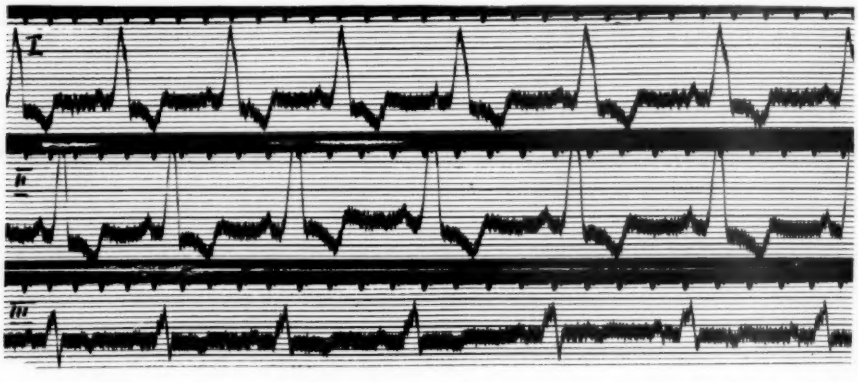


Fig. 2.—Electrocardiogram taken one and one-half hours later. Time marker indicates fifths of seconds.

the mouth was drawn to the right side, and he lost the use of his left arm and leg. After this short periods of consciousness and unconsciousness alternated with complete hemiplegia. Death on November 26, one week after the attack of pain. No post-mortem examination.

COMMENT

It is difficult to correlate the onset of the bundle-branch block with a coronary thrombosis, since the characteristic pain did not occur until forty-five hours later. In view of the subsequent history of what appears quite definitely to be a cardiac infarction with later cerebral embolism from a detached intraventricular thrombus, it is difficult to avoid the conclusion that the electrocardiographic changes were the result of an organic myocardial lesion. Further, in those cases of bundle-branch block in apparently normal healthy adults, which are associated with attacks of paroxysmal tachycardia, reported by Wolff, Parkinson and White,[1] and by Wolferth and Wood,[2] there occurred a

shortening of the P-R interval with the onset of the abnormal ventricular complex. In this case, however, the P-Q interval (which is more strictly comparable) is unchanged by the onset of the bundle-branch block. It is tempting to speculate that the occlusion of the main coronary branch was of slow development and that a deposit of fibrin and platelets occluded a small branch supplying the lower part of the A-V bundle while the first electrocardiogram was being taken, and that the further growth of this thrombus was so slow that the lumen of the main artery was not occluded until forty-five hours later.

REFERENCES

1. Wolff, L., Parkinson, J., and White, P. D.: AM. HEART J. 5: 685, 1930.
2. Wolferth, C. C., and Wood, F. C., AM. HEART J. 8: 297, 1933.

HEMOPERICARDIUM

Report of a Case of Unknown Etiology With Recovery Following Two Pericardial Paracenteses. A Review of the Etiology of Hemopericardium*

Bernard I. Comroe, M.D.
Philadelphia, Pa.

RECENTLY we have had the opportunity to study a patient with a massive hemopericardium. Two pericardial taps were performed with removal of 600 and 900 c.c. respectively of almost pure blood. The patient is in good health one and a half years later.

CASE REPORT

The patient (No. 32-9640), an adult white male, aged fifty-seven years, was referred to the medical service of Dr. Alfred Stengel in the University Hospital from the surgical ward of Dr. E. Eliason, with the chief complaints of weakness, dizziness, and dyspnea. Except for an attack of influenza two months previously, the patient had been well until Feb. 25, 1932. In the afternoon of this date he became dizzy, chilly, and fell backward heavily against a stone wall. Following this he immediately experienced a severe smothering epigastric pain. Extreme dyspnea followed, together with an unproductive cough. This condition persisted until admission a week later. Past medical, family, and social history negative.

Physical examination revealed temperature 99°, pulse 100, respiration 16, blood pressure 130 mm. systolic and 90 diastolic, orthopnea, and marked cyanosis. The cervical veins were greatly distended bilaterally, and many fine râles were heard throughout the chest. The apex beat was not palpable, and the cardiac dullness was greatly increased, extending from 8 cm. to the right of the midline to the left anterior axillary line. No murmurs or thrills were elicited, and heart sounds were barely audible. The liver was tender and enlarged, extending from 4 to 5 finger-breadths below the right costal margin. A small mass was felt in the left upper quadrant, which was probably spleen. The extremities were negative except for a slight amount of dependent edema.

Blood count showed a marked secondary anemia with a moderate polymorphonuclear leucocytosis. The urine contained many red blood cells. A pericardial paracentesis was done with removal of 600 c.c. of bloody fluid. This contained hemoglobin in a concentration of 48 per cent (Sahli) at a time when the hemoglobin of the peripheral blood was 55 per cent.

Following the tap, marked subjective improvement was noticed as well as a definite reduction in the cardiac silhouette both on physical and roentgenological examination (Figs. 1 and 2). On culture the fluid was sterile, and guinea pig inoculations were negative for tuberculosis. Two days later a reaccumulation necessitated a second pericardial tap with withdrawal of 900 c.c. of bloody fluid which had a hemoglobin content of 20 per cent and gave a red blood count of 1,250,000 cells per c.mm. No cholesterol crystals were seen. An attempt to produce a diagnostic pneumopericardium was unsuccessful, the air entering the pleural cavity whence

*From the Medical Clinic of the Hospital of the University of Pennsylvania.

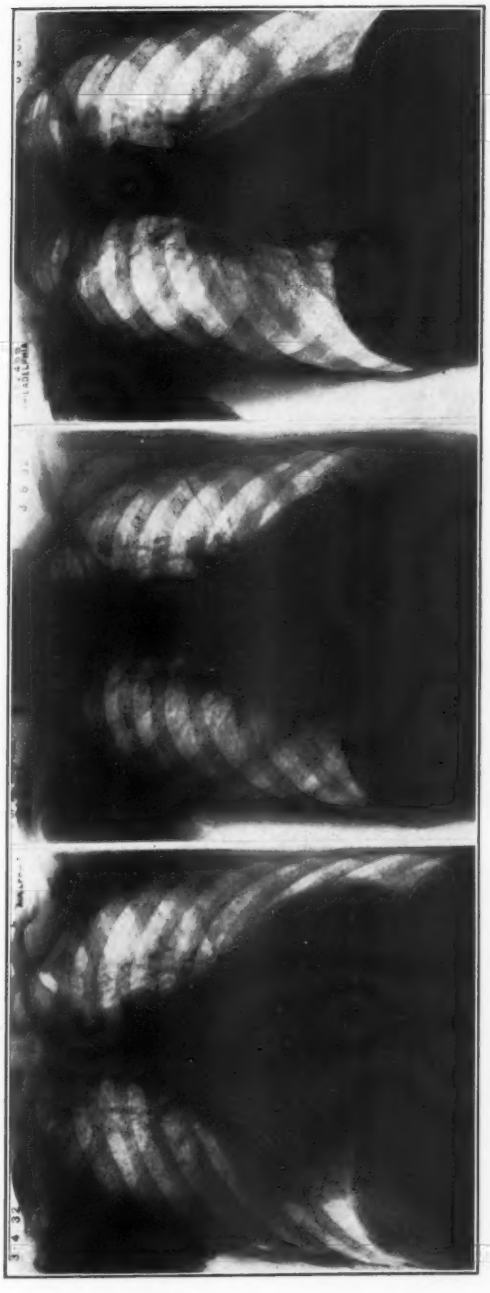


Fig. 3.

Fig. 2.

Fig. 1.

it was slowly absorbed. The patient gradually improved and was discharged in eight weeks, symptom free, with a normal sized heart (Fig. 3) and after absorption of the remainder of the pericardial fluid.

Numerous laboratory examinations were made. In summary these were: negative blood Wassermann with all antigens, normal blood cholesterol, sugar, and urea

nitrogen, and normal phenolsulphonephthalein excretion. Repeated urine examinations for tubercle bacilli were negative. Fragility of the red blood cells was somewhat increased, hemolysis beginning at 0.525 and being complete at 0.425; reticulocyte count was 3.4 per cent. Bleeding and clotting times and clot retraction were within normal limits. The van den Bergh test showed a negative direct reaction, and an indirect reading of 0.2 units. Icterus index was 10. Roentgen examinations of the skull, spine, pelvis, femora, and ribs were negative for any evidence of malignant disease. Intravenous urogram, done because of the persistence of red blood cells in the urine, was negative; however, a retrograde pyelogram of the left urinary tract showed a slight irregularity in the lower calices suggesting a possible pyelonephritis. An electrocardiogram contained some auricular extrasystoles, slurring of the QRS complexes and slight evidence of myocardial damage.

During hospitalization, the temperature was practically normal at all times; the pulse, however, remained between 100 and 110. On discharge, red blood count was 4,500,000, hemoglobin 88 per cent, and white blood cells 9,000, with a normal differential picture. Urine was negative except for a few red blood cells.

A "follow-up" in September, 1933, showed the patient to be in good general health with a normal tolerance for exercise. The heart was not enlarged (by percussion, roentgenogram, or orthodiagram), the sounds were of good quality, and no murmurs or thrills were found. The second aortic sound was moderately accentuated. An electrocardiogram again revealed some evidence of myocardial damage. Blood pressure was 210 mm. systolic, and 100 diastolic, as compared with his previously normal readings. Abdominal examination revealed the liver extending from 4 to 5 fingerbreadths below the right costal margin and firm, smooth, and not tender. The spleen was barely palpable. No other abnormal abdominal masses could be felt. Because of his freedom from symptoms, the patient could not be induced to return to the hospital for further studies.

DISCUSSION

Based on the reported cases, the causes of hemopericardium include the following: (1) tuberculosis[1-11]; (2) rupture of sclerotic coronary vessels[12-14]; (3) wounds of the heart or aorta, and rupture of an aneurysm[15-23]; (4) neoplasms[24-30]; (5) hemorrhagic diseases[31-34]; (6) a postinfectious sequel[35, 36]; (7) chronic nephritis.[37, 38]

Tuberculous pericarditis is not infrequently accompanied by a hemorrhagic effusion. This has seldom consisted of whole blood; moreover the prognosis is usually fatal, with a life expectancy of from one to twelve months from the date of discovery of the effusion. In a recent review by Kornblum et al.[6] of 17 cases of tuberculous pericarditis, only one patient is said to have had bloody fluid.

Rupture of sclerotic coronary vessels with production of hemopericardium has usually been recognized only post-mortem. Alcott[13] in a review of the literature found only 31 cases of rupture of one or both coronary arteries. It is unlikely that this would occur without some associated change in the electrocardiographic findings. No disturbances of note were found in the electrocardiograms of our patient.

Traumatic wounds of the heart, pericardium or aorta are not uncommon. It seems unlikely, however, that the slight fall against the

wall which our patient experienced was responsible for a traumatic wound of these parts. During the past decade, ruptured aneurysms have become a rarity.

Tumors of the heart and pericardium are rare and are usually without symptoms. Only one record has been found of a primary tumor of the heart diagnosed during life.[25] Primary tumors of the pericardium are usually sarcoma or lipoma, although rare instances of carcinoma and endothelioma have been reported. Hemorrhagic effusion is not uncommon from pericardial or cardiac neoplasms. Tumors of any of the organs may give rise to metastasis to the heart. However, the duration of life is usually short and reaccumulation of fluid is rapid.

Practically every hemorrhagic disease has been reported in association with hemopericardium. Leucemia, purpura hemorrhagica, hemophilia, and primary anemia can easily be ruled out by appropriate blood studies. History of adequate diet and lack of other symptoms makes scurvy improbable in our patient. In view of the slight reticulocytosis, and increased fragility of the red blood cells to hypotonic salt solution, the enlarged liver and palpable spleen, hemolytic ictero-anemia is a definite possibility. However, urobilin could be demonstrated at no time in the urine, and the van den Bergh test showed no essential change. If this be the correct diagnosis, the occurrence of a hemopericardium with no other signs of hemorrhage is extremely unusual.

Pericardial effusion secondary to chronic nephritis is usually straw colored or very slightly hemorrhagic. In only 1 of 18 autopsied cases of pericarditis in chronic nephritis did Barach[38] find a frankly bloody fluid.

Another possibility which has been suggested is the simultaneous occurrence of multiple angiomas, liver, pericardium, and other organs being affected. This possibility could not be tested in our patient without exploration, which was refused by the patient.

The cause of the bloody effusion in our patient remains unknown; however, in spite of an almost normal electrocardiogram, we are inclined to believe that the hemopericardium resulted from rupture of a sclerotic coronary vessel in a hypertensive individual.

The diagnostic features of hemopericardium, apart from the character of the fluid, are in no outstanding way different from those of a serous effusion. Tapping when necessary to relieve cardiac tamponade is best performed just outside the apex or in the costoxiphoid angle.

Although the prognosis is poor, with a fatal termination in the large majority of cases, yet numerous reports of cure following evacuation of a hemopericardium can be found.[8, 36, 39, 42]

SUMMARY

1. A case with massive pericardial effusion of blood is reported with a clinical cure following two paracenteses with removal in all of 1,500 c.c. of almost undiluted blood.

2. The etiology of hemopericardium is briefly reviewed.

REFERENCES

1. Hirtz, E.: Pericardite hemorrhagique de nature tuberculeuse, Rev. gén. de clin. et de thérap. **12:** 689, 1898.
2. Souques, M. A.: Pericardite hemorrhagique d'origine tuberculeuse, Bull. Soc. Anat. de Paris **64:** 611, 1889.
3. Hedblom, C.: Primary Tuberculous Pericarditis, S. Clinics N. America **1:** 1411, 1921.
4. Riesman, D.: Primary Tuberculosis of the Pericardium, Am. J. M. Sc. **122:** 6, 1901.
5. Dillon, E. S.: Tuberculous Pericarditis With Tuberculosis of the Myo- and Endocardium, M. Clin. N. America **10:** 253, 1926.
6. Kornblum, K., Bellett, S., and Ostrum, H. W.: Roentgenologic Significance of Tuberculous Pericarditis, Am. J. Roentgenol. **29:** 203, 1933.
7. Hudelo: Pericardite hemorrhagique chez un tuberculeux (epanchement de deux litres; ponction du pericarde), Bull. Soc. Anat. de Paris **63:** 1024, 1888.
8. Hughes, T. A., and Yusuf, M.: Pericarditis With Effusion With Infarction of the Heart in Young Phthisical Subject, Brit. M. J. **1:** 794, 1931.
9. Monnier and Durbin: Pericardite tuberculeuse hemorrhagique, Gaz. med. de Nantes **25:** 15, 1907.
10. Amandrut: Cure of Tuberculous Pericarditis With Bloody Effusion, Bull. et mém. Soc. d. hôp. de Paris **47:** 816, 1923.
11. Waller, W. E.: Tuberculosis of the Pericardium, Lancet **2:** 278, 1923.
12. Edwards, A. T.: Hemorrhage in the Pericardium, M. J. Australia **2:** 761, 1928.
13. Alcott, C. T.: Rupture of Coronary Artery; Hemopericardium, Report of Case and Review of Literature, New England M. J. **204:** 760, 1931.
14. Jones-Evans, E. J. L.: Hemopericardium Resulting From Rupture of the Right Coronary Artery Secondary to Chronic Interstitial Nephritis, Practitioner **109:** 184, 1922.
15. Williamson, A. J.: An Unusual Case of Hemopericardium, Lancet **2:** 1743, 1909.
16. Bird, U. S.: Hemorrhage Into the Pericardium, M. Rec. N. Y. **52:** 701, 1897.
17. Evans, W. A.: Some Cases of Hemopericardium, Birmingham M. Rev. **26:** 20, 1889.
18. Dyson, J. M. and Schnabel, T. G.: Pericardial Hemorrhage—Aneurysm of Aorta With Rupture, Pennsylvania M. J. **35:** 27, 1931.
19. Naismith, W. J.: On the Symptom of Pain in Slow Pericardial Hemorrhage, Lancet **2:** 949, 1889.
20. Warrington: Hemorrhage Into the Pericardium, Liverpool M. Chir. J. **24:** 128, 1904.
21. de Massary, E., and Boquien, Y.: Infarct of the Myocardium With Hemopericardium, Bull. et mém. Soc. med. d. hôp. de Paris **53:** 1430, 1929.
22. Fahr, T.: Fatal Hemorrhage in Heart Following Therapeutic Injections of Drugs and Puncture of Pericardium for Drainage, Deutsche med. Wchnschr. **54:** 1550, 1928.
23. Pallasse, E., and Lambert, M.: Aortic Aneurysm of Dissecting Form With Hemopericardium, Lyon méd. **141:** 519, 1928.
24. Hill, H.: Primary Round Cell Sarcoma of the Pericardium, Arch. Path. **5:** 626, 1928.
25. Yater, W. M.: Tumors of the Heart and Pericardium, Arch. Int. Med. **48:** 627, 1931.
26. Collins, M.: Large Lipoma of Epicardium, Gior. di clin. med. **12:** 1324, 1931.
27. Campagna, M., and Hauser, G. H.: Cancer of Epicardium, J. A. M. A. **90:** 1362, 1928.
28. Keller, W. L., and Callender, G. R.: Neurofibroma Arising on Pericardial Pleura, Tr. Am. Surg. Assn. 474, 1930.

29. Businco, A.: Fibroepithelial Tumors of the Inner Layer of the Pericardium, Tumori 10: 99, 1923. Ab. J. A. M. A. 81: 1244, 1923.
30. Everingham, S.: Primary Endothelioma of the Pericardium, S. Clin. N. America 11: 975, 1931.
31. Abeille: De la pericardite hemorrhagique liee au scorbut; ses points de separation de la pericardite ordinaire, et surtout de la pericardite hemorrhagique par violence hyperemique; trois observations, Gaz. d. hôp. Par. 26: 283, 1853.
32. Vance, B. M., and Graham, J. E.: Periarteritis nodosa complicated by intrapericardial hemorrhage, Arch. Path. 12: 521, 1931.
33. Eshner, A. A.: Hemorrhagic Pericarditis, Tr. Path. Soc. Philadelphia, 1887-89, 14: 155, 1891.
34. Nordmann, M.: Two Cases of Profuse Diapedesis With Effusion Into the Pericardium and Fatal Outcome, Deutsches Arch. f. klin. Med. 147: 100, 1925.
35. Dowd, C. N.: Pericardotomy for Hemorrhagic Pericarditis, Ann. Surg. 57: 768, 1913.
36. Sears, G. G.: A Case of Hemorrhagic Pericarditis Due to Pneumococcus; Aspiration; Recovery, Boston M. & S. J. 139: 293, 1898.
37. Ledoux, S.: Pericardite hemorrhagique du cours d'un mal de Bright, J. d. sc. med. de Lille 1: 80, 1900.
38. Barach, A. L.: Pericarditis in Chronic Nephritis, Am. J. M. Sc. 163: 44, 1922.
39. Stewart, W.: Notes of a Case of Hemorrhagic Pericarditis Associated With Presence of B. Coli Communis; Paracentesis; Recovery, Edinburgh J. M. n.s. 15: 158, 1904.
40. Mores, J. L.: A Case of Traumatic Hemopericardium, Boston M. & S. J. 150: 240, 1904.
41. Bryant, F.: Report of a Case of Hemorrhagic Pericarditis; Aspiration; Recovery, Boston M. & S. J. 152: 521, 1905.
42. Shattuck, F. C.: Pericarditis With Large Hemorrhagic Effusion in a Patient With Grave's disease; Repeated Puncture; Double Dry Pleurisy; Recovery, Boston M. & S. J. 125: 491, 1891.

SYPHILITIC AORTITIS WITH ANEURYSM OF THE INNOMINATE ARTERY AND OCCLUSION OF THE LEFT COMMON CAROTID ARTERY*

LAURENCE E. COOLEY, M.D., AND FRANK P. MCNAMARA, M.D.
DUBUQUE, IOWA

OCCLUSION of the mouths of the coronary arteries due to syphilis is not an uncommon pathological finding. Syphilitic occlusion of larger arteries would seem to be a much rarer condition.

Recently Motley and Moore[1] reported a case of syphilitic aortitis in which the opening of the left common carotid and subclavian arteries "would not much more than accommodate the shaft of a small pin." They mentioned similar reports of syphilitic occlusion made by Preisdorfer[2] in 1878 and Darling and Clark[3] in 1915. Several other reports of syphilitic occlusion were found in the older literature. In 1882 Whitney and Blake[4] described a case of aneurysm of the innominate artery with the orifice of the left common carotid artery only 2 mm. in diameter and the orifice of the left subclavian artery entirely obliterated. In 1885 Suckling and Dendy[5] reported a case of innominate aneurysm in which the orifice of the left common carotid artery was obliterated, while Blackman[6] reported an innominate and aortic aneurysm in which the opening of the left subclavian artery was a "mere chink." In 1902 while discussing surgery of aneurysms Fenger[7] wrote, "In some cases of aneurysm of the aorta as well as the innominate artery the left common carotid artery is either obliterated or very weak." Kaufmann[8] states that occasionally the larger vessels of the arch of the aorta are narrowed or occluded in syphilis of the aorta.

CASE REPORT

A white laborer, aged sixty-two years, came under observation in May, 1932, complaining of a dull aching pain in the left shoulder and arm, and a loss of forty pounds of weight. The onset was insidious and the symptoms had been noticed for one year. Relatives reported that the patient's mental reactions had become much slower during the past five years and that he had complained of being dizzy at times during the past three years.

There was no history of previous illness. The family history was not known. There were two children living and well. The wife was in good health. She had had no miscarriages or stillbirths. There was no history of venereal disease.

Physical examination: The patient was a well-developed male, rather thin, and not acutely ill. The pupils were unequal and irregular and did not react to light. Under the right sternoclavicular joint a pulsating tumor could be felt. No arterial

*From the Departments of Medicine and Pathology, Finley Hospital, Dubuque, Iowa.

pulsation could be palpated on either side of the neck. The sternal ends of both clavicles were enlarged and tender. In the first interspace to the right of the sternum a soft blowing to-and-fro systolic and diastolic murmur could be heard. There was no increase in the supracardiac dullness. Examination of the heart, abdomen, and nervous system revealed no abnormal findings. On the prepuce of the penis was a small whitish scar. There was some limitation of motion of the right elbow and shoulder. There was no arterial pulsation to be obtained anywhere along the right arm or at the wrist. The nails of the right hand were slightly cyanotic. Blood pressure, right arm 0, left arm 96/50. Fluoroscopy of the chest showed a diffuse pulsating enlargement of the arch of the aorta. There were

Fig. 1.—Photograph of heart and great vessels: (*a*) dilated ascending aorta; (*b*) aneurysm of innominate artery; (*c*) thrombosed right common carotid artery; (*d*) subclavian artery and thyroid axis; (*e*) occluded left common carotid artery; (*f*) enlarged left subclavian artery.

no pathological findings in the x-ray pictures of the right shoulder and elbow and in the urine and blood Wassermann examinations.

The patient was given mild antisyphilitic treatment for the next six weeks with some improvement at first. On May 27, 1932, the blood pressure was 70/56 in the right arm and 126/54 in the left arm. At the end of six weeks the patient was too weak to come into the office for treatment. He was next seen September 15, 1932. The pulsating tumor was visible above the right sternoclavicular joint. The patient was not seen again until April 12, 1933. The pulsating tumor could be seen to extend 3 cm. above the clavicle and was 3 cm. in diameter. During the two months preceding, when the patient turned on his left side he had a sensation of smothering and began to lose consciousness. This was promptly relieved when the patient was turned on his back again. He died April 14, 1933.

The points of special interest at autopsy were: a moderate diffuse dilatation of the ascending and transverse aorta with fine linear striations characteristic of luetic mesoaortitis; a diffuse dilatation of the innominate artery, the length being 6 cm. and the diameter 2.5 cm.; an old organized thrombus, found in the upper part of the innominate aneurysm, and a fresher thrombus found in the lower part; organized and canalized thrombi in the right common carotid artery and the right subclavian artery and all its branches except the inferior thyroid; absence of the orifice of the left common carotid artery, represented by a depression in the wall of the aorta; above the occlusion an organized thrombus which extended to the bifurcation into the internal and external carotid arteries; an unusually large left subclavian artery; and an osteochondritis of the sternal ends of both clavicles. Microscopically the aorta and innominate artery showed areas of perivascular round cell infiltration and an increase in the scar and connective tissue with fragmentation of elastic tissue; the orifice of the left common carotid artery was occluded by connective tissue infiltrated with nests of round cells about the blood vessels; hyalinization and round cell infiltration were seen around many of the vessels in the region of the pons; in the testes there was a diffuse increase of connective tissue between the tubules. These were interpreted as the results of syphilis.

COMMENT

This case presented many interesting pathological changes. The blood supply was one of the most remarkable features. Almost no blood reached the head through the right common carotid and right vertebral arteries and none through the left common carotid artery. At autopsy the heart, aorta and as much of the neck as possible were removed *in toto*. Unfortunately we did not suspect the occlusive lesion until the arteries were dissected out several days later. There was no evidence of thrombosis in the left internal and external carotid arteries. It is probable that blood from the left subclavian reached these arteries through the deep cervical artery by an anastomosis with the descending branch of the occipital artery, which is a branch of the external carotid artery. The symptoms of dizziness, retarded mental reactions and the sensation of smothering when lying on the left side can easily be explained on the basis of this unusual blood supply. It seems remarkable that the patient could live at all with such a large part of the ordinary blood supply obstructed.

There have been many reports of aneurysm of the innominate artery associated with syphilis of the aorta. Reviewing the older literature one may say that syphilitic occlusion of the larger branches of the aortic arch also is not an extremely rare pathological finding. Darling and Clark[3] concluded from their study that occlusions of the carotid, innominate, subclavian, renal or mesenteric arteries occurred in 3.7 per cent of syphilitic cadavers. Perhaps a more diligent search at autopsy would lead to similar reports now.

Clinical diagnosis of these occlusive lesions may be made if one has this possibility in mind when examining cases of syphilis of the cardiovascular system. Certainly it is easy to determine whether or not

there is a pulsation in the carotid and subclavian arteries. Vague and unusual symptoms may thus be explained. Finally a correlation of autopsy findings and clinical symptoms may lead to the formation of a definite symptom-complex in syphilitic occlusions of the larger branches of the aorta.

REFERENCES

1. Motley, Lyle, and Moore, Robert: Obliterating Syphilitic Arteritis, J. A. M. A. **100**: 656, 1933.
2. Preisdorfer, P.: Virchow's Arch. f. path. Anat., 1878, p. 73 (quoted by Motley and Moore[1]).
3. Darling, S. T., and Clark, H. C.: Arteritis Syphilitica Obliterans, J. M. Res. 32: 1, 1915.
4. Blake, John G., reported by Mr. H. B. Whitney: Aneurysm of the Innominate, Boston M. & S. J. **106**: 418, 1882.
5. Suckling, R., and Dendy, W.: A Case of Innominate Aneurysm, Lancet **2**: 245, 1885.
6. Blackman, J. G.: Diffused Innominate Aneurysm, Lancet **1**: 928, 1887.
7. Fenger, Christian: Aneurysm of the Innominate Artery, Med. Standard **25**: 12, 1902.
8. Kaufmann, E.: Lehrbuch der Speziellen Pathologischen Anatomie, Berlin und Leipzig, 1922, p. 93, Vereinigung Wissenshaftlicher Verleger.

Department of Reviews and Abstracts

Selected Abstracts

Hart, Andrew D., Wood, J. Edwin, and Daughton, A. D.: Rheumatic Fever in Piedmont, Virginia. I. Incidence and Clinical Manifestations. Am. J. M. Sc. **187:** 352, 1934.

Two hundred instances of rheumatic disease observed during a six-year period at the University of Virginia Hospital have been studied in an effort to determine the approximate incidence of the disease as a whole and to note particularly the relative occurrence of its various manifestations.

It would appear that rheumatic fever is of frequent occurrence in central Piedmont, Virginia, where it is three times as common as in the tidewater section of the same state. The arthritic forms of the disease, although mild and of such short duration as to suggest that they may at times escape detection, are relatively frequent and tend to recur in a fairly high percentage of cases. Serious and permanent damage to the heart is evidenced in a surprisingly large number of persons with rheumatic fever.

Elliot, Albert H.: Anemia as the Cause of Angina Pectoris in the Presence of Healthy Coronary Arteries and Aorta: Report of a Case. Am. J. M. Sc. **187:** 185, 1934.

A fifty-five-year-old woman with chronic anemia and repeated epistaxes had attacks of angina pectoris over a period of three years which became extremely severe with the occurrence of a febrile illness. At necropsy an hypertrophied but otherwise normal heart was found. The coronary arteries were thin walled and dilated; detailed study revealed no lesions in their walls other than occasional flecks of lipoid on the intima; the aorta was unchanged. The physiological evidence is reviewed which indicates that anemia, by increasing cardiac output, may cause myocardial hypertrophy; that under these circumstances the adaptive limit of the coronary flow may be reached in the resting state and easily exceeded under additional physiological circulatory burden and that the resultant myocardial ischemia might express itself as an anginal seizure. It is suggested that such a mechanism could well explain both the clinical and the pathological findings in this case. This study demonstrates that angina pectoris may occur in the absence of disease of the coronary arteries, myocardium or aorta.

Laplace, Louis B., and Crane, Martin P.: Observations on the Production of Pain and Fatigue in Muscular Ischemia and Their Relationship in Angina Pectoris. Am. J. M. Sc. **187:** 264, 1934.

Observations were made in a series of 36 subjects on the relationship of ischemia to the development of pain and fatigue in the contracting muscles of the arm. The development of both pain and fatigue was favored by arrest of the circulation, but the two phenomena were not affected to the same extent by dif-

ferent degrees of ischemia or by variations in the type of work. In many cases the relatively early development of fatigue was able to terminate exercise before the manifestation of severe pain. Constitutional nervous sensitivity did not appear to affect the pain of muscular ischemia.

On the basis of these observations, it is concluded that constitutional nervous sensitivity is unlikely to be a significant factor in the occurrence of angina pectoris. The rarity of cardiac pain in congestive heart failure and its absence in many cases of coronary obstruction may be explained by the fact that the development of cardiac fatigue maintains the maximal work of the heart at a level below the threshold of pain production.

Levy, Robert L., Bruenn, Howard G., and Kurtz, Dorothy: Facts on Disease of the Coronary Arteries, Based on a Survey of the Clinical and Pathologic Records of 762 Cases. Am. J. M. Sc. **187**: 376, 1934.

A statistical analysis was made of the autopsy and clinical records of 762 cases of coronary artery disease observed at the Presbyterian Hospital during the period from 1910 to 1931. The facts apparent as a result of this survey are to be regarded as applying to this material; no general conclusions are drawn.

Arteriosclerosis was the most common lesion, having been found in 97.2 per cent of the cases. Syphilitic aortitis, by inducing stenosis or occlusion of the coronary orifices, was responsible for impairing the coronary blood flow in 5.7 per cent. Syphilis did not play a rôle in predisposing to coronary sclerosis. It was present no more frequently in patients with coronary disease than in those without it.

In 2,877 consecutive autopsies, lesions of the coronary arteries were found in 25.9 per cent. This is a strikingly high figure.

In half of the cases showing sclerosis in the coronaries, the lesions were "slight" or "moderate"; in many of these instances, no functional impairment of the cardiac circulation was induced by such lesions. The lesser degrees of sclerosis were observed predominantly in the younger age groups; the more marked lesions developing with advancing years.

In this series of autopsies, the incidence of coronary disease showed a slight but steady increase throughout a twenty-two-year period; but the increase was not nearly so great in the proved cases as was indicated by the figures based on clinical diagnosis alone. The reasons in explanation of these facts have been given.

Coronary artery disease increased at all ages, but the increase was particularly noteworthy between the ages of twenty-five and forty-four years. There was a predominance of males. The number of cases increased in both sexes.

Occupation did not appear to play a significant part in determining those whose vessels were affected. The largest percentage of coronary cases was found among foremen and skilled workers.

The clinical diagnosis of coronary disease is being made with greater accuracy as well as with increased frequency. Many cases are latent and probably cannot be recognized during life. Even in the presence of calcification or stenosis, the diagnosis was made clinically in but 16 per cent of the cases during the years from 1920 to 1931. During this same period, coronary thrombosis was correctly diagnosticated in only 43 per cent of the cases.

Arteriosclerotic heart disease was the most frequent primary cause of death. Cardiac insufficiency was the commonest terminal event.

The increase in the incidence of affections of the coronary arteries is not to be regarded as a matter of concern. Rather should it be a source of satisfaction

that, due largely to effective control of infectious diseases, men may survive to an age when disorders incident to senescence lead to the termination of life.

Averbuck, Samuel H.: The Differentiation of Acute Coronary Artery Thrombosis From Pulmonary Embolization. Am. J. M. Sc. **187**: 391, 1934.

Pulmonary embolus may cause a clinical picture indistinguishable from the syndrome of an acute coronary artery thrombosis. The case records and autopsy findings are presented of six patients in whom this problem in diagnosis occurred. In two the conditions coexisted. Some points of possible aid in differentiation are discussed. The possibility of successful surgical removal of pulmonary emboli as well as other differences in treatment makes this problem more than one of purely academic or diagnostic importance.

Blumgart, Herrman L.; Roesler, Hugo; White, Paul D.; Brenner, Oscar; and Cutler, E. C.: Symposium on the Pulmonary Circulation. New England J. Med. **209**: 1259, 1933.

The physiology of the pulmonary circulation was discussed by Dr. Blumgart, in this symposium before the New England Heart Association. Briefly he describes the anatomical distribution of the vessels, the pressure relations within the right side of the heart and the pulmonary circulation and the effect of exercise, respiration and thyroid disease on this circulation.

Dr. Roesler discussed the increasing importance of the x-ray study of the pulmonary circulation. Investigation of the cardiac patient by fluoroscopic study as well as by use of x-ray films was shown to reveal important changes in the hilar shadows and the pulmonary artery. The importance of pulmonary hypertension is becoming more evident, particularly in relation to left heart failure. Such studies are also valuable in congenital heart disease.

Dr. White and Dr. Brenner discussed the pathological and clinical aspects of the pulmonary circulation. Three general conclusions to be drawn from the report are as follows: (1) All pulmonary blood vessels are subject to a wide variety of pathological conditions; (2) sclerosis is as common in the pulmonary circulation as in the systemic; and (3) the pathology of the pulmonary blood vessels seems to influence very infrequently symptoms, signs, or the clinical course of disease.

Dr. Cutler discussed pulmonary embolectomy. The operative technic is described briefly. It is believed that the operation is indicated when an early diagnosis can be made and when the operation can be performed without delay. Time is the chief factor, and when hospitals are fully prepared to carry out this procedure, more satisfactory results will accrue.

Lamb, Arthur E.: Heart Disease in Pregnancy. Am. J. M. Sc. **187**: 177, 1934.

The incidence of cardiac murmurs in pregnant women in this series was 6.1 per cent. Of these, 2.7 per cent had organic heart disease, while 3.4 per cent had functional murmurs only and no detectable lesion.

The importance of recognizing functional murmurs has been pointed out. None of these patients showed the slightest evidence of cardiac strain during pregnancy, and the follow-up shows that nearly all these functional murmurs disappeared after pregnancy.

The most frequently observed lesion was mitral stenosis with or without insufficiency. One-third of the cases of mitral stenosis decompensated, while no case of uncomplicated mitral insufficiency decompensated, demonstrating the importance of differentiating between these two lesions.

The functional classification of pregnant cardiac patients has been considered, and it was noted that 5 cases out of Classes 1 and 2 (a) decompensated, which is at variance with the work of Pardee who claims that Classes 1 and 2 (a) have an excellent prognosis. Other factors, in the author's opinion, must be considered in addition to the functional classification, such as the age of the patient, the family environment, the duration of the heart disease, and the extent of valvular damage.

Most of the cases that decompensated did so before the onset of labor, and there was no relationship demonstrated between the month of pregnancy and the onset of decompensation.

The mortality was 7.5 per cent, which falls within the mortality range of from 5 to 10 per cent as reported by reliable observers. Two of these deaths were probably preventable. Consideration of the mortality of the patients having prenatal care and those who did not, shows a death rate of 2.2 per cent in the former and in the latter 20 per cent, thus demonstrating the importance of prenatal care.

The limited follow-up showed that 56 per cent were not worse following pregnancy, while 43 per cent were. The need for further follow-up study to determine what happens to the cardiac mother and her child after the lying-in period is obvious.

Master, Arthur M.: Right Ventricular Preponderance of the Heart. The significance of Ventricular Preponderance and T-Wave Inversion in the Human Electrocardiogram. Am. J. M. Sc. **186**: 714, 1933.

Electrocardiograms from 173 cases in the last four years showing right ventricular preponderance of the QRS group were studied. The groups of diseases found to be associated with right ventricular preponderance are: (1) chronic valvular disease (57 per cent) with mitral stenosis alone or associated with other valvular lesions; (2) degenerative heart disease (21 per cent); (3) noncardiac diseases such as thyroid disease, bronchial asthma and emphysema and finally congenital heart disease and syphilis. Female individuals predominated in patients with chronic valvular disease and male individuals in the degenerative heart disease group.

Right ventricular preponderance with inversion of T_2 and T_3 is associated with the most marked right ventricular enlargement, with the largest hearts, with the most marked enlargement of the pulmonary conus and the left auricle, with markedly increased lung markings and congestion in the lungs and with the highest mortality (33 per cent). Right ventricular preponderance with inversion of T_3 alone is associated with a less marked degree of these anatomical changes and a mortality of 15 per cent and finally in right ventricular preponderance with any inversion of the T-wave at all, the least changes occur and the mortality is only 7 per cent.

Auricular fibrillation was present in 40 per cent of the patients showing right ventricular preponderance with both T_2 and T_3 inverted, 17 per cent when T_3 alone was inverted, and only 7 per cent with no T-wave inversion.

Kissin, Milton, Ackerman, Walter, and Katz, Louis N.: The Effect of the Heart's Position on the Electrocardiographic Appearance of Bundle-Branch Block in Man. Am. J. M. Sc. **186**: 721, 1933.

The present investigation was made to discover whether changes in the heart's position caused a noticeable shift of the electrical axis in six individuals with so-called right bundle-branch block. Electrocardiograms were taken in various positions of the body and in different phases of respiration. Some degree of

shift in electrical axis appeared with change in position of the heart in every case. Twice, marked changes in the electrical axis appeared, and the electrocardiogram of a so-called right bundle-branch block changed to the indeterminate type of bundle-branch block. The position of the heart as well as the site of the blocked bundle-branch determine the direction of the QRS of the electrocardiogram of bundle-branch block. This may be the explanation of certain apparent contradictions in the findings of previous students of bundle-branch block.

It is suggested that electrocardiograms heretofore interpreted as left and right bundle-branch block be reported simply as intraventricular block or "bundle-branch block configuration" and that no attempt be made to locate the blocked bundle-branch from the electrocardiographic appearance alone.

France, Richard: The Large Q-Wave in Lead III of the Electrocardiogram. Am. J. M. Sc. **187:** 16, 1934.

An analysis is made of 103 electrocardiograms characterized by a normal sinus rhythm with a significant Q-wave in Lead III. A study of the histories of the cases with reference to the electrocardiographic findings is presented. The pathological alterations in the hearts of 12 of the cases are given. The relation of the Q-wave mechanism to occlusion of the right coronary artery and infarction of the posterior basal portion of the interventricular septum is discussed.

The results of the present study are in accord with the observations of others to the effect that the large Q-wave in Lead III while sometimes present in the absence of heart disease, is frequently associated with serious myocardial damage. Furthermore, it is indicated that when this wave and additional evidence of myocardial disease exist in the record, angina pectoris is often present. Postmortem findings support the view that the deep Q_3 is commonly seen as part of the evidence of the electrocardiographic change occurring after thrombosis of the right coronary artery with subsequent infarction of the posterior base of the left ventricle and adjacent portion of the interventricular septum.

Bunta, Emil: Blood Pressure Variations in Tuberculosis. Am. Rev. Tuberc. **29:** 335, 1934.

The object of the present study was to determine the range of arterial tension in tuberculosis. A greater divergence from the range of absolute normal pressures was noted in tuberculous than in normal patients with the same sex, age, and weight. It was found that pulse pressures manifest the widest variations chiefly at the expense of systolic pressures. Variations from normal arterial tension are directed mostly toward hypotension levels. The trend in tuberculosis is toward relative hypotension rather than absolute hypotension levels. Conspicuous hypotension pressures are predicated on either pathological extent or clinical activity of tuberculous lesions. Of the two factors, clinical activity is the principal determinant. Progressive lowering pressures especially pulse pressures, parallel tuberculous activity, the degree of which is enhanced as the disease approaches the far advanced stage.

The practical import of these considerations is their application in the diagnosis, prognosis, and treatment of tuberculous patients. From a diagnostic point of view, blood pressure observations are chiefly useful as clues or as confirmatory facts in the evaluation of clinical data. The trend of recurrent individual measurements toward normal findings speaks well for ultimate arrest of the disease. A progressive lowering of blood pressure, especially pulse pressure, calls for a guarded prognosis. The management of tuberculous patients, based on a program

of rest or exercise, discontinuance or resumption of employment, preference of dispensary supervision or sanatorium care, depends in no small measure on information derived from the individual blood pressure record.

Berconsky, Isaac: The Blood-Respiratory Function in Black Cardiacs of Ayerza. Semana med. **1:** 1569, 1933.

This study is based on ten patients with so-called Ayerza's disease (cardiacos negroes of Ayerza). These patients had an old chronic bronchopulmonary process with emphysema and developed an intense cyanosis without evident cardiac insufficiency as a cause of the cyanosis. Unless interrupted by an intercurrent process, six patients after several years showed a congestive cardiac failure which in several of the cases became the cause of their death.

Argentine authors, pupils of Professor Ayerza, as well as authors of other countries, attribute the intense cyanosis and other symptoms and signs which these patients present, chiefly to a sclerosis of a branch of the pulmonary artery, to the cardiac failure, or to the reduction of the alveolar field in the lungs. According to the determinations carried out by the writer, it was found that due to the rigidity of the thorax, the vital capacity of these subjects is diminished strongly between 40 and 68 per cent of normal. Since the tidal flow of air is also low, there is an alveolar hypoventilation with diminution of the oxygen alveolar tension (average 64, 33 mm. Hg) with a rise in the tension of carbon dioxide (average 63, 27 mm. Hg). The low alveolar oxygen tension is the reason for the low arterial saturation (average 77, 92 per cent). The rise of the alveolar CO_2 tension determines the carbon dioxide excess (high alkaline reserve with P_H normal) and serves as a compensating measure. The great quantity of the arterial reduced hemoglobin found also in the capillary vessels (average 7.46 grams) explains logically the cyanosis (cyanosis arterial). Factors which help to intensify the cyanosis are the increased quantity of hemoglobin existing, the rise of CO_2, and the development of a dilated capillary bed which these patients present. When the cardiac insufficiency appears, the cyanosis tends to be intensified, due to the circulatory congestion (cyanosis mixta). The inhalation of oxygen will modify the arterial cyanosis.

The writer concludes that the cyanosis which is a symptom whereby the condition is called cardiacos negros is due to alveolar hypoventilation.

Eppinger, Eugene C., and Midelfart, Peter A. H.: Stenosis of the Isthmus (Coarctation) of the Aorta. Am. J. M. Sc. **185:** 528, 1933.

Three typical cases of coarctation of the aorta are presented and discussed briefly with emphasis on the history and physical findings. The salient point to be drawn from these cases is the fact that evidence of hypertension or hypertensive disease in a young adult without renal disease should suggest the possibility of coarctation of the aorta before considering the case as one of idiopathic hypertension. A less important though none the less striking feature is intermittent claudication of the legs in the same period of life.

Book Review

DIE TONUSKRANKHEITEN DES HERZENS UND DER GEFÄSSE: IHRE BIOLOGIE UND THERAPIE. By Dr. J. Pal. Julius Springer, Vienna, 1934. 228 pages and 20 illustrations.

In this monograph Professor Pal succeeds in combining a discussion of the biological basis of variations in muscle tone—particularly in muscle tone as it affects the heart and blood vessels—and a practical handbook written with clinical insight. In the first part of the book Dr. Pal discusses the cellular basis of tonicity, a function which he ascribes to the sarcoplasm as opposed to the kinetic function of the fibrillae of the muscle cells. He then considers the variations in tone of the heart and vessels, in health and in disease, as regulated by the nervous system and as affected by toxins and by drugs. In the second part of the book he turns to the clinical picture resulting from hyper- and hypotonicity. Particularly interesting is his discussion of primary permanent hypertonicity of the arteries, which he considers as an independent, usually hereditary, disease of the blood vessels, leading to hypertension ("essential hypertension"), hypertrophy of the heart, arterial and arteriolar sclerosis, and other anatomical changes. He stresses the importance of the psychic factor on p. 134, saying: "The majority of patients with hypertonicity have—as long as they know nothing of their illness—no, or only slight, subjective symptoms. As soon as they learn that their condition is not normal, they feel sick, complain of their troubles and seek to find complaints. They are sick nervously and should be treated accordingly." Dr. Pal takes up the symptoms, complications, treament and prognosis, emphasizing the fact that many members of hypertensive families live to old age. The entire book gives evidence of the author's wide reading, independent work, and wise clinical viewpoint.

E. H.